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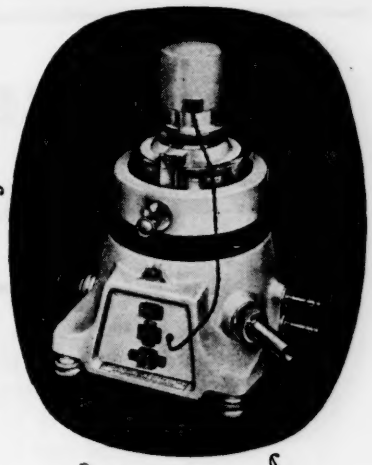

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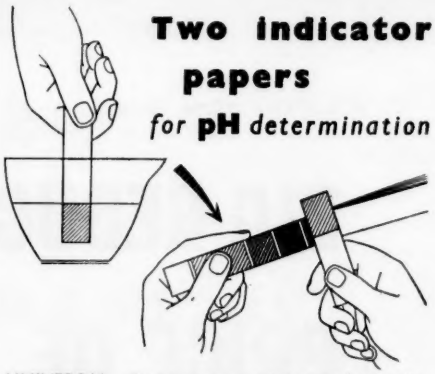

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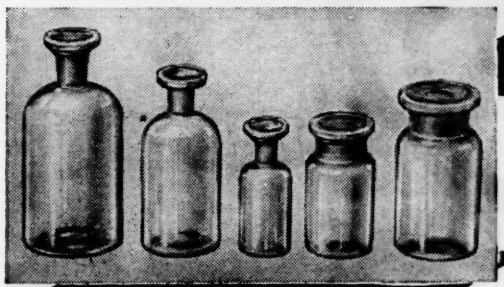

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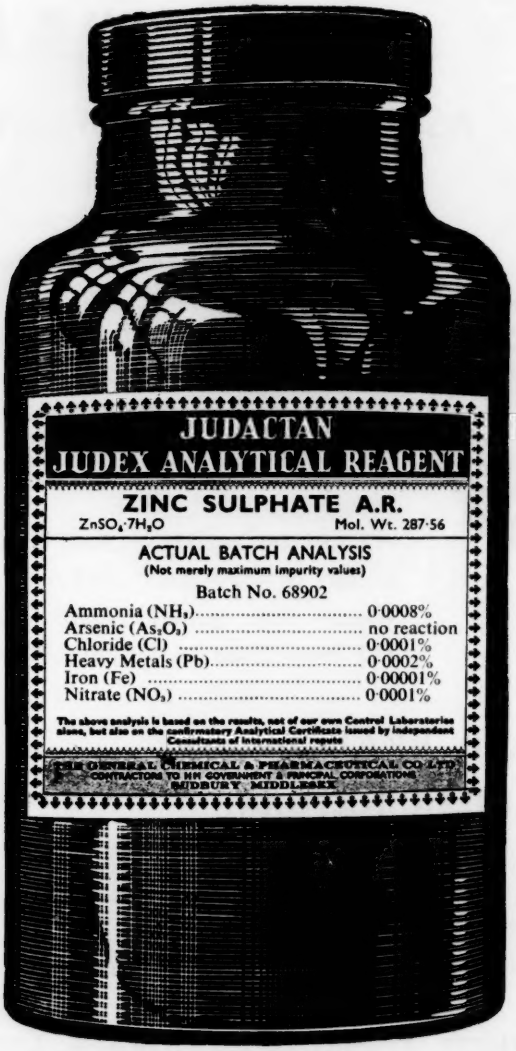
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The Friedel–Crafts Reaction in the Carbazole Series. Part IV. Phenylacetyl Compounds.*

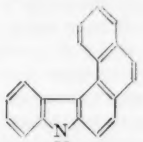
By D. A. KINSLEY and S. G. P. PLANT.

[Reprint Order No. 5009.]

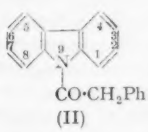
The 1-, 2-, and 3-phenylacetyl derivatives of carbazole, in addition to 3 : 6-bisphenylacetylcarbazole, have been prepared, and their structures established by conversion into known carbazolecarboxylic acids. Several derivatives of these ketones have been obtained, and attempts have been made to convert 3-phenethylcarbazole into naphtho(2′ : 1′-3 : 4)carbazole.

FOR the preparation of naphtho(2′ : 1′-3 : 4)carbazole (I) it seemed that advantage might be taken of the experience recorded in the previous Parts, in which it was found that 3 : 6-diacylcarbazoles are readily obtained from carbazole and the 2-acyl derivatives from 9-acylcarbazoles, by the Friedel–Crafts reaction, while the 3-acylcarbazoles can be obtained by the action of aluminium chloride on the 9-acyl compounds.

9-Phenylacetylcarbazole (II) was prepared by the action of phenylacetyl chloride on 9-carbazolylmagnesium iodide and was heated with aluminium chloride with the formation of 3-phenylacetylcarbazole, together with a little of the isomeric 1-acyl compound. This conforms with Meitzner's observation (*J. Amer. Chem. Soc.*, 1935, **57**, 2327) that 1-acetylcarbazole accompanies the 3-acetyl compound obtained by a similar process. 3-Phenethylcarbazole (III) was prepared from the corresponding ketone by Huang-Minlon's method (*J. Amer. Chem. Soc.*, 1946, **68**, 2487), but attempts to effect cyclodehydrogenation of this substance under various conditions with the formation of (I) have been unsuccessful. Efforts to obtain 9-*o*-nitrophenylacetylcarbazole, in the hope that the phenanthrene system in (I) might ultimately be formed from a reduction product of its isomer by an application of Pschorr's reaction, also failed.



(I)



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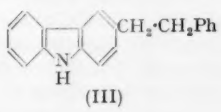

(III)

3 : 6-Bisphenylacetylcarbazole has been obtained by applying the Friedel–Crafts reaction to both carbazole and its 3-phenylacetyl derivative, and has been reduced to 3 : 6-diphenethylcarbazole by the Clemmensen method. The 3 : 6-bisphenylacetyl derivative of 9-methylcarbazole has been obtained by the Friedel–Crafts method as well as by methylation of the above diketone, but attempts to obtain 9-methyl-3-phenylacetylcarbazole by the use of a unimolecular proportion of phenylacetyl chloride gave mixtures. The compound was more conveniently prepared by the methylation of 3-phenylacetylcarbazole. It is of interest in this connexion that Buu-Hoï and Royer (*J. Org. Chem.*, 1951, **16**, 1198) have prepared the 9-*n*-butyl and 9-*iso*amyl derivatives of 3-phenylacetylcarbazole from the appropriate 9-alkylcarbazoles by the Friedel–Crafts method.

2-Phenylacetylcarbazole and its 9-benzoyl derivative have been obtained from the product of a Friedel–Crafts reaction with 9-benzoylcarbazole. The structures of all the above ketones were established by converting the key substances into known carbazolecarboxylic acids by fusion with potassium hydroxide.

EXPERIMENTAL

9-Phenylacetylcarbazole.—After magnesium (1·2 g.) had reacted with methyl iodide (7·1 g.) in dry ether (100 c.c.), carbazole (6 g.) was gradually added and the whole refluxed for 10 min.

* Part III, *J.*, 1947, 937.

Phenylacetyl chloride (7·7 g.) in ether was added in portions with frequent agitation of the syrupy layer, and the whole again refluxed for 10 min. Part of the product was isolated from the ethereal layer after the latter had been washed with dilute hydrochloric acid and dried ($MgSO_4$), and the remainder by treatment of the residual oil with dilute hydrochloric acid. When the whole was crystallised from ethanol, 9-*phenylacetylcarbazole* was obtained in pink plates (5 g.), m. p. 112°. It then separated from acetic acid in colourless plates, m. p. 114° (Found: C, 84·3; H, 5·3. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3%). It was hydrolysed to carbazole when refluxed with aqueous ethanolic potassium hydroxide for 5 min.

3-*Phenylacetylcarbazole*.—After a mixture of 9-phenylacetylcarbazole (16 g.), aluminium chloride (8·5 g.), and nitrobenzene (160 c.c.) had been gradually brought to 120° and kept at that temperature for 15 min., it was cooled, poured into dilute hydrochloric acid, and the nitrobenzene removed in steam. When the solid residue was dried, distilled under reduced pressure, and crystallised twice from ethanol, 3-*phenylacetylcarbazole* (5 g.) was obtained in plates, m. p. 164° (Found: C, 84·3; H, 5·2%). Its *oxime* crystallised from ethanol in needles, m. p. 214° (Found: C, 80·2; H, 5·3. $C_{20}H_{16}ON_2$ requires C, 80·0; H, 5·3%). Its *phenylhydrazone*, plates, m. p. 239° (from ethanol), was obtained when the ketone (0·5 g.) was heated with phenylhydrazine (1 g.) at 150° for ½ hr. and the mixture treated with carbon tetrachloride (Found: C, 83·5; H, 5·5. $C_{26}H_{21}N_3$ requires C, 83·2; H, 5·6%).

When gradually added to a hot molten mixture of potassium hydroxide (10 g.) and water (1 c.c.), 3-phenylacetylcarbazole (1 g.) dissolved to form a yellow solution. After the aqueous solution of the cold mass had been filtered and acidified with hydrochloric acid, the solid was obtained from acetic acid in plates, m. p. 270°. It was shown to be carbazole-3-carboxylic acid by mixed m. p. and by conversion into its ethyl ester, m. p. 164°, not depressed by admixture with an authentic sample (Plant and Williams, *J.*, 1934, 1142).

After 3-phenylacetylcarbazole (1·9 g.) in acetone (10 c.c.) containing sodium hydroxide (2·3 g.) in water (1·3 g.) had been shaken with methyl sulphate (2 c.c.) for a few minutes, addition of water precipitated an oil which was extracted with carbon tetrachloride. When the extract was dried ($MgSO_4$) and evaporated, the residue, which slowly solidified, gave 9-*methyl*-3-*phenylacetylcarbazole* (0·8 g.) in clusters of pale yellow prisms, m. p. 114°, after being washed with carbon tetrachloride and twice recrystallised from ethanol (Found: C, 84·1; H, 5·8. $C_{21}H_{17}ON$ requires C, 84·3; H, 5·7%). Prepared similarly by using acetyl chloride instead of methyl sulphate, 9-*acetyl*-3-*phenylacetylcarbazole* separated from ethanol in needles, m. p. 113·5° (Found: C, 80·7; H, 5·1. $C_{22}H_{17}O_2N$ requires C, 80·7; H, 5·2%), and gave 3-phenylacetylcarbazole on being refluxed with aqueous ethanolic potassium hydroxide.

1-*Phenylacetylcarbazole*.—When the mother-liquors from the crystallisation of 3-phenylacetylcarbazole referred to above were evaporated and the residue recrystallised from a little ethanol, more 3-phenylacetylcarbazole separated in clusters of plates admixed with yellow needles, m. p. 120—124°, of 1-*phenylacetylcarbazole*, which on occasions could be removed by hand. More conveniently, the residue was ground with carbon tetrachloride (150 c.c.). The insoluble material was reasonably pure 3-phenylacetylcarbazole (about 1·5 g.). When the filtered solution was passed through alumina (4 × 1 cm.) to remove dark coloured material and evaporated, treatment of the residue with ethanol gave 1-phenylacetylcarbazole (1 g.), m. p. 119—122°. Crystallisation from ethanol gave golden needles, m. p. 119·5—123·5°, which, after adsorption on alumina, had m. p. 123—124° (Found: C, 84·1; H, 5·3%). Its *oxime* crystallised from carbon tetrachloride in needles, m. p. 122° (Found: C, 80·2; H, 5·5%). When heated with molten potassium hydroxide as described for the isomeric ketone, carbazole-1-carboxylic acid, m. p. 267° with slight previous softening, identical (mixed m. p.) with an authentic sample (Briscoe and Plant, *J.*, 1928, 1990), was formed.

3-*Phenethylcarbazole*.—A mixture of 3-phenylacetylcarbazole (3 g.), powdered potassium hydroxide (2 g.), hydrazine hydrate (1·2 c.c.; 100%), and diethylene glycol (12·3 c.c.) was heated under reflux at 140—165° for 1½ hr., and then at 185—205° for 4 hr. without the reflux condenser. When the solid obtained by stirring the cold residue with water was crystallised from ethanol, 3-*phenethylcarbazole* was isolated in plates (2 g.), m. p. 213° (Found: C, 88·7; H, 6·3. $C_{20}H_{17}N$ requires C, 88·6; H, 6·3%).

Methyl sulphate (1 c.c.) in acetone (3 c.c.) was gradually added to a boiling mixture of 3-phenethylcarbazole (0·5 g.), sodium hydroxide (1·3 g.), water (0·5 c.c.), and acetone (5 c.c.), and the whole boiled for 5 min. with shaking. Addition of water precipitated 9-*methyl*-3-*phenethylcarbazole*, grey prisms (0·3 g.), m. p. 89° (from ethanol) (Found: C, 88·2; H, 6·9. $C_{21}H_{19}N$ requires C, 88·4; H, 6·7%).

3 : 6-*Bisphenylacetylcarbazole*.—Phenylacetyl chloride (4 g.) was added to a mixture of

carbazole (2 g.), powdered aluminium chloride (3·5 g.), and dry benzene (30 c.c.), with shaking, and the whole left for 12 hr. with exclusion of moisture, and poured into dilute hydrochloric acid. After removal of the benzene in steam, treatment of the solid residue with acetone gave 3 : 6-*bisphenylacetylcarbazole*, which crystallised from nitrobenzene in grey plates (1·5 g.), m. p. 228—236°. Further crystallisation from dioxan and then anisole gave colourless plates, m. p. 242° with slight previous softening (Found : C, 83·5; H, 5·4. $C_{28}H_{21}O_2N$ requires C, 83·4; H, 5·2%). The same compound was prepared by a similar method from 3-phenylacetylcarbazole. After being heated with molten potassium hydroxide as described for 3-phenylacetylcarbazole, this diketone gave an acid which was treated with ethanolic hydrogen chloride with the formation of diethyl carbazole-3 : 6-dicarboxylate, m. p. 202°, identical (mixed m. p.) with an authentic sample (Mitchell and Plant, *J.*, 1936, 1295).

Prepared from the diketone by a method similar to that used for 9-methyl-3-phenylacetylcarbazole, 9-*methyl*-3 : 6-*bisphenylacetylcarbazole* was crystallised from acetic acid and then from ethanol, and obtained in needles, m. p. 145° (Found : C, 83·5; H, 5·8. $C_{29}H_{23}O_2N$ requires C, 83·4; H, 5·5%). This compound (mixed m. p.) was also easily obtained from 9-methylcarbazole by the action of phenylacetyl chloride and aluminium chloride as described above for the unmethylated compound; for purification it was necessary only to crystallise the crude product from ethanol.

After 3 : 6-bisphenylacetylcarbazole (2 g.) in acetone (40 c.c.) containing powdered potassium hydroxide (7 g.) had been shaken for 10 min. with acetyl chloride (10 c.c.), water precipitated 9-*acetyl*-3 : 6-*bisphenylacetylcarbazole*, needles (1 g.), m. p. 157° (from acetic acid and then ethanol) (Found : C, 80·8; H, 5·1. $C_{30}H_{23}O_3N$ requires C, 80·9; H, 5·2%). It gave 3 : 6-bisphenylacetylcarbazole when refluxed for 1 hr. with aqueous ethanolic potassium hydroxide.

3 : 6-*Diphenethylcarbazole*.—A mixture of 3 : 6-bisphenylacetylcarbazole (3 g.), glacial acetic acid (60 c.c.), and amalgamated granulated zinc (90 g.) was refluxed while concentrated hydrochloric acid (60 c.c.) was added in portions during 6 hr. After the liquid had been removed by decantation and the residue extracted with acetic acid, water was added to the combined solution, and the product extracted with carbon tetrachloride. The extract was washed with aqueous sodium carbonate, dried ($MgSO_4$), and evaporated. The residue, which slowly solidified, was ground with a little carbon tetrachloride and crystallised from acetic acid, from which 3 : 6-*diphenethylcarbazole* separated in needles (0·7 g.), m. p. 145° (Found : C, 89·7; H, 6·6. $C_{28}H_{25}N$ requires C, 89·6; H, 6·7%).

2-*Phenylacetylcarbazole*.—After a mixture of 9-benzoylcarbazole (15 g.), aluminium chloride (45 g.), phenylacetyl chloride (26 c.c.), and carbon disulphide (120 c.c.) had been refluxed for 1¼ hr. and the solvent distilled off, the residue was added to dilute hydrochloric acid, and the product extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, then with aqueous sodium carbonate, dried ($MgSO_4$), and evaporated. When the orange coloured gum was dissolved in benzene (250 c.c.) and adsorbed on alumina, elution with benzene gave first 9-*benzoyl*-2-*phenylacetylcarbazole* (about 1·5 g.), colourless rhombs, m. p. 183—185° after slight softening from 179° (from benzene) (Found : C, 83·2; H, 4·9; N, 3·7. $C_{27}H_{19}O_2N$ requires C, 83·3; H, 4·9; N, 3·6%), and then 2-*phenylacetylcarbazole* (about 0·5 g.), colourless plates, m. p. 209—211° (rapid heating) (from ethanol) (Found : C, 83·7; H, 5·5; N, 5·1. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3; N, 4·9%). The former was converted into the latter either by adsorption on more alumina or by refluxing it with aqueous ethanolic potassium hydroxide.

When 2-phenylacetylcarbazole was heated with molten potassium hydroxide as described for the 3-phenylacetyl compound, carbazole-2-carboxylic acid, m. p. 320° with previous softening, was obtained. It was identified by mixed m. p. and by conversion into its ethyl ester, m. p. 181—183°, not depressed by admixture with an authentic sample (Plant and Williams, *loc. cit.*).

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 5th*, 1954.]

Properties of Actomyosin before and after Treatment with Ion-exchange Resins: Influence of pH *and Ionic Strength on Molecular Shape of a Structural Muscle Protein.*

By M. L. R. Harkness and A. Wassermann.

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Actomyosin before and after treatment with ion-exchange resins is characterised by ash content, analysis, solubility, qualitative flow birefringence tests, electrophoretic migration, light scattering, and intrinsic viscosity. An attempt to explain the properties of the protein in terms of a reversible polymerisation reaction, the solute being taken to be a rigid structure, was incompatible with results of light-scattering and viscosity measurements. A consistent explanation can be given if it is postulated that actomyosin, in dilute solution, is composed of flexible chains, the shape of which depends on pH and ionic strength of the solvent. The order of magnitude of the average distance between the chain ends is estimated.

It is important to know whether filamentous structural muscle proteins, in dilute solution, can be regarded as (*a*) rigid structures or (*b*) flexible chains capable of marked changes of configuration under appropriate chemical conditions. These macromolecular ampholytes have been frequently investigated (for references see Bailey, *Adv. Protein Chem.*, 1944, **1**, 289; Weber and Portzehl, *ibid.*, 1952, **7**, 161), but a convincing decision between the two possibilities has not been made. The present work deals with actomyosin (for nomenclature, see *idem*, *ibid.*), because it is a representative filamentous muscle protein and may play a significant rôle in the process of muscular activity. If actomyosin is prepared according to standard methods (*e.g.*, Greenstein and Edsall, *J. Biol. Chem.*, 1940, **133**, 397) it retains about 1% of ash (see Dubuisson, *Arch. Int. Physiol.*, 1941, **51**, 136) and it is sparingly soluble, between pH 4·0 and 9·0, in water or in salt solutions of ionic strength $\mu \leqslant 0{\cdot}3$. It will be shown in this paper that the ash content of actomyosin can be reduced to less than 0·02% by treatment with ion-exchange resins, and that the demineralised protein is easily soluble in water of pH $< 4{\cdot}8$ and $> 6{\cdot}5$. Owing to the increased solubility, comparative tests, including light-scattering experiments, could be carried out upon actomyosin dissolved in both pure water and potassium salt solutions. The results favour hypothesis (*b*), the biological implications of which were pointed out by Meyer (*Biochem. Z.*, 1929, **214**, 272) and later by others.

The present conclusions relate to dilute solutions of actomyosin and are not relevant for the problem of protein structure in concentrated solutions, or in the dry state, where the molecules may be arranged in helical shape. No evidence is available to show that such configurations play a rôle in dilute sols; moreover, the light-scattering and the hydrodynamic treatment of helices have not yet been developed and they are not considered here. The molecular weight or length of actomyosin has not been determined accurately but their order of magnitude could be computed. These results relate to "unfractionated" protein, made by a technique outlined below. It is not suggested that this material and actomyosin prepared by other techniques are of similar size and shape. The light scattering by solutions of actomyosin has so far only been measured by the transmission method. Investigations dealing with the angular distribution of scattered light and with "fractions" of actomyosin in solutions of various simple salts will be described in other papers.

Experimental

Reactions with Ion-exchange Resins.—Actomyosin was extracted from the hind-leg muscles of rabbits, according to Singher and Meister (*J. Biol. Chem.*, 1945, **159**, 419; Singher, Ph.D. Thesis, Harvard University, 1944, "method 4"). In most experiments the sol–gel conversion of the protein was brought about by controlled dialysis at 0°; the outer solution, three times renewed, was water or potassium veronal buffer ($\mu = 0{\cdot}0025$) of pH = 7·8; the ratio v = total volume of outer solution/volume of protein sol was 20—50, and the time, t, of the dialysis was 7—15 hr.

The gel was centrifuged (3000 ***g***.) at 0° for 1 hr. and redissolved in a potassium chloride–bicarbonate buffer of pH 7·8 (μ_{KCl} and μ_{KHCO_3} of the sol being respectively 0·500 and 0·0400), a second precipitation being brought about by dialysis as described. The centrifuged, fully swollen gel (I) was redissolved in the specified potassium chloride–bicarbonate buffer and precipitated by prolonged dialysis against five-times renewed water at 0° ($v = 200$; $t = 50$—60 hr.), the centrifuged gel being designated by (II). The measurements to be described were done not later than 5 days after the preparation of these gels, all protein preparations being stored at 0°. The water was distilled from an all-glass apparatus; control tests showed that no significant change of the properties of actomyosin occurs if the water had been redistilled from an all-silica still of the type described by Weber (*Z. Naturforsch.*, 1949, **4**b, 124).

The following ion-exchange resins were used : A = Amberlite IR-100 or IR-120, strong acids in the hydrogen form; B = Dowex-2, a strong base in the hydroxide form; C = Dowex-2 in the acetate form; D = Amberlite IR-4, a weaker base in the carbonate form. The resins were washed with pure water immediately before use, until the specific conductance of the filtrate was less than 10^{-6} ohm^{-1} cm.$^{-1}$, at 20°. In each run a suction-dry aliquot portion of the washed resin was tested for dry weight and total exchange capacity. In preliminary tests (I) was stirred with a mechanical mixture of A and B; under these conditions insoluble isoelectric actomyosin is formed which cannot easily be separated without considerable loss. In other tests (I) was treated successively with (1) B and A; (2) A, B, and A; (3) A and D; (4) C, A, and B; the concentration and time conditions being given in Table 1. The first resin treatment caused

TABLE 1. *Experimental conditions in reactions between actomyosin and ion-exchange resins.*

Sequence of application of resin	G. of actomyosin in 100 cm.^{3} of reaction mixture	G. of dry ion-exchanger per g. of dry actomyosin				Time of contact (min.) between ion-exchanger and actomyosin				pH of solution after treatment with resin			
		A	B	C	D	A	B	C	D	A	B	C	D
B, A	0·3—0·9	10—90	10—70	—	—	30—180	45—720	—	—	4·1—4·2	10·5—11·3	—	—
A, B, A	0·5	11(55) *	11	—	—	75(210) *	5	—	—	3·5	4·5	—	—
A, D	0·3—0·4	55—220	—	—	24—55	20—60	—	—	20	3·5	—	—	4·2
C, A, B	0·3	40	40	30	—	30	5	75	—	4·0	4·2	8·1	—

* Numbers in parentheses relate to second resin treatment.

dissolution of the protein, and no precipitation occurred in the later stages, so the separation from the resins could be done by filtration. These reactions occurred in a static system at 0°, with stirring, except in the last stages of procedure (4), in which the sol was passed through a bed of the resin under conditions similar to those prevailing in chromatographic adsorption. Atmospheric carbon dioxide had no significant influence, as established by control experiments in which regeneration of the resins, interaction with (I), filtration, and washing of the residue with water were done in an atmosphere of pure nitrogen. Procedure (4), in which the pH remained within the range 4·0—8·1, was selected for the preparation of the demineralised actomyosin sols, used for all the following experiments. After the final filtration, the sol was centrifuged and stored in silica containers at 0° (sol III).

TABLE 2. *Composition of actomyosin gels.*

Treatment of actomyosin with ion exchanger	Sample obtained from	No. of samples analysed	Equiv. of KCl per 100 g. of fully swollen centrifuged gel	C, %	H, %	N, %	K, %	Cl, %	Ash, %
				in dry gel					
	Gel (I)	11	~0·02	47·1 ± 0·6	7·3 ± 0·2	13·6 ± 0·4	10·9 ± 0·4	3·6 ± 1·4	>2
—	Gel (II)	2	<0·001	50·9 ± 0·5	7·2 ± 0·3	15·8 ± 0·4	<0·1	1·1 ± 0·5	1·5 ± 0·5
+	Sol (III)	8	—	49·7 ± 0·6	7·3 ± 0·3	15·5 ± 0·4	—	1·6 ± 0·6	<0·02

Analytical and pH *Measurements.*—The concentration of sols or gels with respect to actomyosin was determined by the micro-Kjehldahl method with the precautions described by Chibnall, Rees, and Williams (*Biochem. J.*, 1943, **37**, 354), and 15·8% nitrogen content being

assumed. This is the mean of figures given by Greenstein and Edsall (*loc. cit.*), Dubuisson (*loc. cit.*), Szent-Gyöergy (*Acta Physiol. Scand.*, **1945**, Suppl. 25), and of those given in col. 7 of Table 2, the latter analyses relating to actomyosin which had not been treated with organic solvents before the drying operation (0·5 mm. pressure, first at room temperature and finally at 80°). Potassium was estimated according to Tisdale and Kramer after digestion according to Abelin (*Helv. Chim. Acta*, **1941**, **24**, 611), other analyses being done according to Pregl. The potassium chloride content of gels (I) and (II) was estimated conductometrically or by pH determination after interaction with resin A.

The pH measurements were made with a Cambridge Instrument Company meter in conjunction with the vessel shown in Fig. 1. In the electrometric titrations the reference electrode was in contact with the magnetically stirred sol. If, on the other hand, a solution of actomyosin in water, of specified pH, but free from potassium chloride, was required, suction was applied at (6) and, by operation of tap (7), the sol could be introduced into the burette (5), which was removed and quickly connected, by means of the standard joint, with the head of a viscometer or with an optical or conductivity cell. The opening (8) was closed, the reference electrode was pushed down, thereby bringing it in contact with the remaining sol in the vessel, and the pH was determined. The vessel was swept by nitrogen, so that no significant uptake of carbon dioxide occurred during the few seconds between the removal of (5) and the

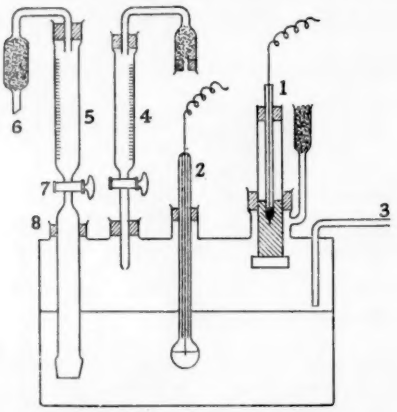


FIG. 1. *Reaction vessel used for* pH *measurements and for preparation of actomyosin sols.*

(1) Saturated potassium chloride calomel reference electrode.
(2) Glass electrode.
(3) Inlet tubing for flushing vessel with pure nitrogen.
(4) Microburette for addition of potassium hydroxide or hydrochloric acid solutions.
(5) Burette used for the transfer of protein sols.

closing of (8). A mechanical mixture of thoroughly washed ion-exchange resins A and B was suspended in the lower part of a burette, which was fitted to the opening (8). By percolating distilled water through the resin mixture a protein sol could be diluted with a known volume of pure water, without simultaneous uptake of carbon dioxide.

Qualitative Flow-birefringence Tests.—These were carried out according to Edsall and Mehl (*J. Biol. Chem.*, **1940**, **133**, 409).

Electrical Conductivity.—Sols and gels were introduced into cells the constants of which were respectively 0·0430 and 1·48 $cm.^{-1}$. The platinum electrodes were lightly platinised, and the construction of the cells was such that dilution could be done in the cell, without uptake of atmospheric carbon dioxide. The bridge arrangement for measuring the resistance was similar to that described by Shedlovsky (*J. Amer. Chem. Soc.*, 1930, **52**, 1793).

Electrophoretic Migration.—This was measured in a Tiselius apparatus. The sols were centrifuged at 12,000—20,000 ***g*** (0°) and equilibrated, at 0°, against the relevant buffer solutions. Boundaries were photographed with red light, Ilford H P 3 plates being used.

Light Absorption and Scattering.—The experiments were done with the help of a Unicam SP. 500 spectrophotometer, turbidities being determined at least at five wave-lengths (350—700 mμ) by the transmission method (Doty and Steiner, *J. Chem. Phys.*, 1950, **18**, 1214) with the necessary precautions as to slit-width adjustments and with a set of optical cells, varying in length from 0·2 to 10 cm.; some of the cells could be evacuated and the sols could be introduced without bringing them into contact with atmospheric carbon dioxide. The sols, containing not more than 0·6% of actomyosin, had been centrifuged to constant turbidity at 20,000—40,000 ***g*** (0°). In order to avoid a possible contamination by small particles stirred up during the removal of the centrifuge cups and decantation, a final gravity filtration (0°) through sintered-glass

filters was carried out, the concentration of the sol and the porosity of the plate being adjusted in such a way that about 50 cm.^{3} of sol passed the filter in 12 hr., the ratio of surface of filter plate to volume of sol, initially on top of the filter, being 10 cm.$^{-1}$. If the centrifugation of the sols is done at concentrations above 0·6%, or if filtration through sintered-glass filters of smaller porosity is carried out, a fractionation occurs and sols are obtained which contain an actomyosin the weight average molecular weight of which is substantially smaller than that specified below.

Refractivity.—The increments in Table 5 were determined with a differential refractometer having a limiting sensitivity of $\pm 1 \times 10^{-6}$ (McEwan and Pratt, unpublished work). The centrifuged and filtered sols were carefully equilibrated against buffers, the refractive indices of which were measured in a Pulfrich refractometer, mercury, sodium, and cadmium lamps being used. The refractive indices of water were taken from Landolt and Börnstein's tables.

Viscometers.—These were of the type described by Fox, Fox, and Flory (*J. Amer. Chem. Soc.*, **1951**, **73**, 1901), two instruments of the following significant dimensions were used :

	Capillary, cm.		Bulb, cm.^{3}			Capillary, cm.		Bulb, cm.^{3}	
Viscometer	Length	Diameter	Upper	Lower	Viscometer	Length	Diameter	Upper	Lower
1	17·1	0·1509	4·780	4·033	2	24·0	0·06796	3·430	3·176

The kinetic-energy correction, determined by calibration with water or sucrose solution, was less than 2% of the total viscosity, even at the highest rate of shear. Flow times were determined with a calibrated stop-watch, the viscometer being placed in a thermostat, the temperature of which was constant to within $\pm 0·01°$. In carrying out experiments with protein sols at pH >4, both limbs of the viscometer were connected with soda–lime tubes, the carbon dioxide being removed from the empty viscometer by a stream of nitrogen. Burette (5) (Fig. 1) was fitted to the wide limb of the viscometer by way of a T-piece connection. From the moment of introducing the sol into the viscometer until temperature equilibrium was established the sol was kept in continuous motion by sucking it into one of the bulbs and letting it flow down, thereby reducing the influence of thixotropic effects. In runs in which the flow time of the first reading was somewhat greater than that of consecutive readings Bailey and Perry's procedure (*Biochim. Biophys. Acta*, 1947, **1**, 507) was adopted. In determining intrinsic viscosities, the concentration of the sols was adjusted in such a way that the thixotropic effects become negligible at least at the three most dilute solutions. The maximum rate of shear at the wall of the capillary (referred to below as the rate of shear) was calculated as by Fox, Fox, and Flory (*loc. cit.*).

Results

Analytical, Solubility, Flow-birefringence, and Electrochemical Measurements.—The analytical composition and some solubility and flow birefringence properties of actomyosin, before and

Table 3. *Comparison of some properties of actomyosin before and after treatment with ion-exchange resins; temp.*, 20—25°.

Treatment of actomyosin with ion exchanger	pH range	Solvent	Solubility *	Flow birefringence
—	<4	Water, buffer, or salt solns.	+	—
+			+	—
—	4·0—4·8 *	Water	—	
+			+	—
—	4·0—4·8 *	Acetate buffer (μ = 0·02—0·1)	—	
+			+	—
—	4·0—4·8	Salt solns. (μ = 0·05—0·8)	—	
+			—	
—	4·8—6·5	Water, acetate buffer, or salt solns.	—	
+		(μ = 0·05—0·8)	—	
—	6·5—9·0 *	Water	—	
+			+	+
—	6·5—9·0	Salt solns. with or without buffer (μ<0·3)	—	
+			—	
—	6·5—9·0	Salt solns. with or without buffer	+	+
+		(μ>0·35<1)	+	—
—	>9	Water, buffer, or salt solns.	+	—
+			+	—

* + Indicates that no precipitate is formed at 20°, after 24 hr., the concentration of actomyosin being 0·6%; — indicates that the gel–sol conversion is not complete under the same temperature and time conditions, even if the reaction mixture contains only 0·05% of actomyosin.

after treatment with ion-exchange resins, are shown in Tables 2 and 3. Starting materials for these runs were gel (I) or sol (III). The salts referred to in col. 3 of Table 3 are the chlorides of potassium, sodium, calcium, and magnesium; pH values >6·5 were adjusted by veronal or phosphate buffers. Sol (III) does not give a precipitate on addition of acetic acid–potassium acetate buffers within the specified range of pH values and ionic strengths, but precipitation occurs if a phthalic acid–potassium phthalate buffer of pH 4·0 and $\mu = 0{\cdot}030$ is added. The pH ranges 4·0—4·8 and 6·5—9·0 are marked in Table 3 with an asterisk, because they are those in which treatment with ion-exchange resins affects the solubility of actomyosin in the most marked manner. Sol (III) is not detectably flow-birefringent, under the conditions of these qualitative tests, which were done at low rates of shear; flow birefringence could easily be observed, however, if a sufficient amount of potassium hydroxide is added to sol (III) to bring the pH within the range 6·5—9·0; the effect being detectable even if the sol contains only 0·1% of actomyosin. If a strongly flow-birefringent, salt-free sol of pH 6·5—9·0 containing 0·6% of actomyosin is made 0·50M with respect to potassium chloride, the optical anisotropy disappears. Before treatment with the resin, a 0·6% solution of actomyosin in 0·50M-potassium

FIG. 2.

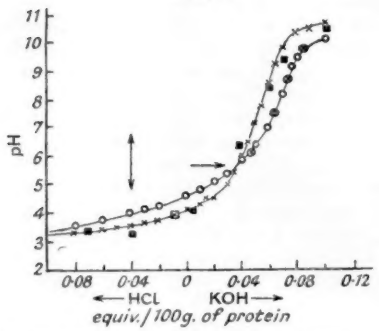


FIG. 3.

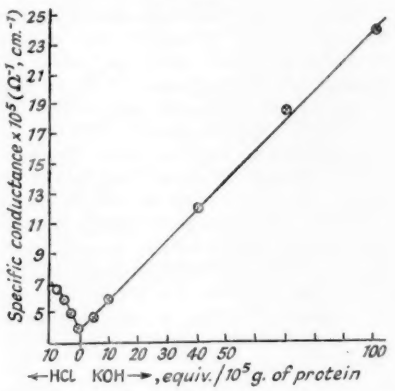


FIG. 2. *Electrometric titration of actomyosin sols before and after treatment with ion-exchange resins.*

×, ○, ⊗, ⊠, After treatment with ion-exchange resins; starting material sol (III); temp. 18·0°. Initial and final protein concentration 0·150 and 0·132 g./100 cm.³ of solution.

×, Solvent, water; ○, □, solvent, 0·500M-KCl.

⊗, Sol (III) was brought to pH 10·5; after 5 min. at this pH the lower pH values were reached by back-titration with HCl.

⊠, Sol (III) was brought to pH 3·1; after 5 min. at this pH the higher pH values were reached by back-titration with KOH. ×, ○, KOH or HCl directly added to Sol (III).

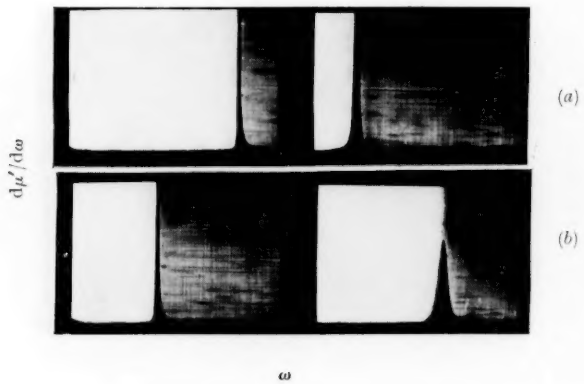
■, Actomyosin which had not been in contact with ion-exchange resins; these results are taken from Dubuisson and Hamoir (*Arch. Int. Physiol.*, 1943, **53**, 313); it has to be taken into account that in these tests the starting material was the isoelectric protein.

FIG. 3. *Conductometric titration of actomyosin after treatment with ion-exchange resins. Starting material: sol* (III). *Temp.*, 0·0°.

chloride is strongly flow-birefringent (cf. Greenstein and Edsall, *loc. cit.*; Edsall and Mehl, *loc. cit.*; Edsall, *J. Biol. Chem.*, 1930, **89**, 289).

Results of electrometric titrations are shown in Fig. 2. Practically identical values were obtained in experiments in which the protein concentration was 0·0520 or 0·635 g./100 cm.³ of sol, or in which the reaction mixture was 0·0204 and 0·102M with respect to potassium chloride. The " intersection points " in these runs corresponded to pH 5·5 or 5·6; the mean of these values, and of that indicated in Fig. 2 by a horizontal arrow, is 5·6. In the case of actomyosin not treated with ion-exchange resins, an " intersection " point of pH 5·5 has been observed (Dubuisson and Hamoir, *loc. cit.*). The vertical arrow in Fig. 2 indicates the approximate pH range in which actomyosin is insoluble. With the protein which had been treated with ion-exchange resins, and in the absence of salts, precipitation and re-solution occur if one passes from pH < 4·8 to > 6·4; this, however, does not give rise to a break in the electrometric or

FIG. 4. *Electrophoretic pattern of actomyosin sols after treatment with ion-exchange resins. Temp.*, 0·5°.



The width of the band, ω, is plotted against the refractive index gradient $d\mu'/d\omega$; potential gradient, 1·24 v/cm.; duration of test 1·5 hr. in (*a*) and 19 hr. in (*b*). Ascending boundary (protein migrates to anode, into the buffer) on left; descending boundary (protein migrates away from buffer) on right. Actomyosin concentration 0·55 g./100 cm.^{3} of solution. pH = 6·60. $\mu_{KCl} = 0{\cdot}335$; $\mu_{K_2HPO_4} = 0{\cdot}0750$; $\mu_{KH_2PO_4} = 0{\cdot}0250$.

To face p. 1349.

conductometric titration curve. Typical results of the latter measurements are in Fig. 3. From these and similar conductometric analyses it can be calculated that sol (III) cannot contain more than 2×10^{-4} mole of free acetic acid per litre, this upper limit being obtained by assuming that the contribution of the protein conductivity is negligible.

The electrophoretic pattern of actomyosin prepared from sol (III) is shown in Fig. 4. The starting solution had been brought to pH 6·60 by addition of potassium hydroxide, potassium chloride and phosphates being subsequently added. A similar pattern was observed with actomyosin which had not been in contact with ion-exchangers. Electrophoretic migration velocities of the principal protein component are in Table 4; the specified inaccuracies of the

TABLE 4. *Electrophoretic migration velocity of actomyosin before and after treatment with ion-exchange resin; temp.*, 0·5°.

Treatment of actomyosin with ion-exchanger	pH	Solvent	Protein concn. (g./100 cm.³ of sol)	Electrophoretic migration velocity × 10^5 (cm.²/v-sec.)
—	6·46	Buffer *A*	0·22	2·26 ± 0·02
	6·46	Buffer *A*	0·30	2·60 ± 0·05
+	6·60	Buffer *B*	0·55	3·24 ± 0·02

Buffer *A* = KCl (μ = 0·500), K_2HPO_4 (μ = 0·0206), KH_2PO_4 (μ = 0·0161).
Buffer *B* = KCl (μ = 0·335), Na_2HPO_4, (μ = 0·0750), KH_2PO_4 (μ = 0·0250).

figures in the last column were computed by taking into account both ascending and descending boundaries.

Turbidities and Refractivities.—To facilitate presentation of results and subsequent discussion, the following relations are mentioned:

$$\tau = (1/d)\ln_e J_0/J = 2{\cdot}30\varepsilon \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(\tau/HC)_{c\to 0} = MQ_{\text{exp.}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$(\tau/HC)_{\substack{c\to 0 \\ \lambda\to\infty}} = M \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$H = (32\pi^3/3N\lambda^4)[(\mu' - \mu_0')/C]^2\mu_0'^2 \text{ and } H\lambda^4 = H'. \quad . \quad . \quad . \quad . \quad (4)$$

$$-\frac{\text{d log } (\tau)_{c\to 0}}{\text{d log } \lambda} + \frac{\text{d log } H'}{\text{d log } \lambda} = 4 - \frac{\text{d log } Q_{\text{exp.}}}{\text{d log } \lambda} = 4 - \beta \quad . \quad . \quad . \quad . \quad (5)$$

$$\text{d log } Q_{\text{theor.}}/\text{d log } \lambda = \beta' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where τ is the turbidity of the actomyosin sols, d the optical path-length, J_0 and J the intensity of incident and transmitted light, C the solute concentration, M the weight-average molecular weight of the solute, N Avogadro's number, λ the wave-length of the light, and μ' and μ_0' the refractive indices of solution and solvent, respectively; $Q_{\text{exp.}}$ and $Q_{\text{theor.}}$ are particle dissipation factors, the former to be experimentally determined from the wave-length dependence of τ and H' and the latter to be calculated from analytical expressions due to Doty and Steiner (*loc. cit.*) and Bucche, Debye, and Cashin (*J. Chem. Physics*, 1951, **19**, 803). Equation (5) is identical with (17) of Doty and Steiner's paper if one neglects d log H'/d log λ; in Doty and Steiner's numerical calculations the term has been taken into account. The dependence of β' on the molecular dimensions becomes negligibly small if the scattering particles are sufficiently large, but the limiting values, β'_∞, depend markedly on the shape of the solute. For this reason a comparison between β and β'_∞ is useful, as shown below, but it does not enable one to compute molecular weight or dimensions. These parameters can be estimated from (3), in conjunction with an extrapolation method proposed by Cashin and Debye (*Phys. Review*, 1949, **75**, 1307), in which $(HC/\tau)_{c\to 0}$ is plotted against $(\mu_0'/\lambda)^2$, thereby obtaining the intercept for $(\mu_0'/\lambda)^2 = 0$. Insertion of the reciprocal of this intercept in (2) gives $Q_{\text{exp.}}$, and comparison with the appropriate value of $Q_{\text{theor.}}$ enables one to calculate the dimension of the solute, the choice of the model to be used for a calculation of $Q_{\text{theor.}}$ being facilitated by comparison between β_∞ and β.

Results of typical experiments showing the dependence of τ/c on the concentration of actomyosin are in Fig. 5; from these and similar measurements the term on the left-hand side of (2) can be estimated. The shape of the graphs in Fig. 5 is typical for all the wave-lengths and solvents. Measurements, similar to those shown by d in Fig. 5, were done with actomyosin prepared from four rabbits, and the following values for $\tau/2{\cdot}30C$ ($C = 5{\cdot}00 \times 10^{-4}$ g./cm.³ of sol) were obtained: **32, 35, 36, 34** cm.²/g. In order to calculate β, (2) is written in the form

$$\log\{(\varepsilon/hc)_{c\to 0}\} + q = \log Q_{\text{exp.}}$$

TABLE 5. *Refractive-index increments of actomyosin sols; temp.*, 20°.

Solvent	pH	Wave-length (mμ)	Refractive-index increment (cm.³/g.)	Solvent	pH	Wave-length (mμ)	Refractive-index increment (cm.³/g.)
Water	4·26	578	0·191 ± 0·002	Buffer *C*	8·26	578	0·203 ± 0·002
		546	0·193 ± 0·002			546	0·205 ± 0·002
		436	0·195 ± 0·002			436	0·208 ± 0·002
Buffer *A*	6·46	578	0·193 ± 0·003				

Buffer *A*: as Table 4.
Buffer *C*: KCl (μ = 0·500), $KHCO_3$ (μ = 0·0400).

where $h = H \times 3N/32\pi^3$ and q is independent of λ. For the sake of simplicity in plotting, a quantity A is defined by

$$A = \log\{(\varepsilon/hc)_{c\to 0}\} + 15{\cdot}00 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

It will be seen that β is the slope of the straight line obtained by plotting A against log λ. Typical graphs of this kind are in Fig. 6. For calculations of h in (7) for different wave-

FIG. 5.

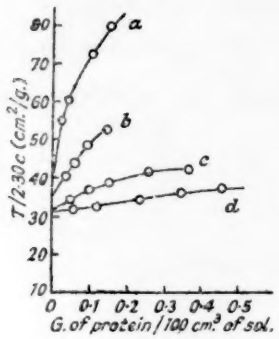


FIG. 6.

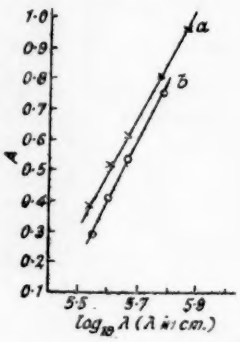


FIG. 5. *Reduced turbidities of actomyosin sols; temp.*, 20°; *wave-length of light*, 589 mμ.

(*a*) Before treatment with ion-exchange resins; starting material gel (I); solvent buffer *A* (see Table 4); pH 6·46; μ = 0·537.
(*b*), (*c*), and (*d*) After treatment with ion-exchange resins.
(*b*) Sol (III) brought to pH 6·46 by addition of KOH; KCl and phosphates subsequently added; solvent and μ as in (*a*).
(*c*) Sol (III) brought to pH 8·80 by addition of KOH; no salt or buffer added.
(*d*) Sol (III); pH 4·26; no salt or buffer added.

FIG. 6. *Light-scattering of actomyosin sols at different wave-lengths; temp.*, 20°.

The significance of the symbol A is given in (7), above, ε/ch being expressed in g. (*a*) and (*b*) relate to the same sols as those specified in the legend of Fig. 5.

TABLE 6. *Results of light-scattering and refractive-index measurements.*

No.	Treatment of acto-myosin with ion-exchanger	Solvent	pH	Ionic strength	$\left(\frac{\tau}{2{\cdot}30C}\right)_{c\to 0}$, in cm.²/g. ($\lambda$ = 589 mμ)	$\left(\frac{10^8 HC}{\tau}\right)_{c\to 0}$, in g.⁻¹ ($\lambda$ = 589 mμ)	Weight-average molecular weight × 10⁻⁸	$\beta = \frac{\Delta \log Q}{\Delta \log \lambda}$	Particle dissipation factor, $Q_{exp.}$ (λ = 589 mμ)
1 *	—	Buffer *A*	6·46	0·537	42 ± 3	3·6 ± 0·2	2 ± 1	1·8 ± 0·3	0·13 ± 0·05
2	—	Buffer *C*	8·26	0·540	55 ± 5	2·7 ± 0·2	2 ± 1	1·5 ± 0·3	0·19 ± 0·08
3	+	Water	4·08	—	31 ± 2	4·2 ± 0·2	1·3 ± 0·4	1·7 ± 0·3	0·18 ± 0·05
4 *	+	Water	4·26	—	30 ± 3	4·1 ± 0·4	1·4 ± 0·5	1·6 ± 0·3	0·18 ± 0·06
5	+	Buffer *D*	4·00	0·100	41 ± 3	3·3 ± 0·2	3·0 ± 1	2·0 ± 0·4	0·10 ± 0·03
6	+	Buffer *A*	6·46	0·537	35 ± 3	4·2 ± 0·4	2·0 ± 0·5	1·7 ± 0·3	0·12 ± 0·04
7	+	Buffer *C*	8·26	0·540	34 ± 2	4·3 ± 0·3	2·0 ± 0·5	1·8 ± 0·3	0·12 ± 0·04
8	+	Water	7·88	—	45 ± 3	2·9 ± 0·2	2·0 ± 0·5	1·8 ± 0·3	0·17 ± 0·04
9	+	Water	8·88	—	32 ± 3	4·0 ± 0·4	2·0 ± 0·5	1·7 ± 0·3	0·13 ± 0·04

Buffers *A* and *C* as Tables 4 and 5; buffer *D* = acetic acid–potassium acetate.
* These experiments were done in duplicate.

lengths, the refractive index increments were determined at different concentration of actomyosin in the range 0·103—0·412%. The results of these measurements are in Table 5; in no case could a detectable concentration dependence of the increments be observed. These measurements were done with actomyosin after treatment with ion-exchangers: comparison with unpublished work of Dr. P. Johnson shows that the interaction with the resins has no significant influence on the increment. The increments shown in Table 5 were converted into other wave-lengths, within the range specified before, by an interpolation or extrapolation method similar to that of Perlman and Longsworth (*J. Amer. Chem. Soc.*, 1948, **70**, 2719). The various β values in col. 9 of Table 6 were calculated from graphs similar to those shown in Fig. 6. The weight-average molecular weight, M, of actomyosin is listed in column 8 of Table 6. These values were deduced from the intercept of such graphs as those shown in Fig. 7. The slopes of these graphs, $S = (\lambda/\mu_0')^2(HC/\tau)_{c\rightarrow 0}$, are $0{\cdot}62 \times 10^{-16}$ and $0{\cdot}77 \times 10^{-16}$ cm.²/g. The mean S value of all the experiments listed in Table 6 is $(0{\cdot}6 \pm 0{\cdot}2) \times 10^{-16}$ cm.²/g. No significant relation could be detected between the numerical value of S and pH, ionic strength, or other chemical conditions.

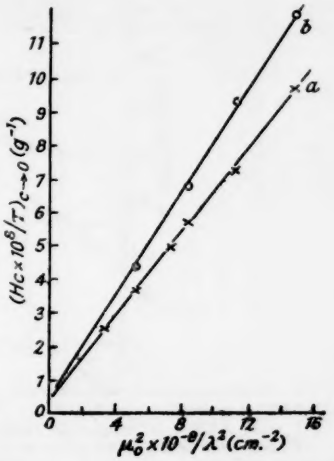


FIG. 7. *Typical graphs used for estimation of weight-average molecule weight of actomyosin.*

(*a*) and (*b*) relate to the sols specified in the legend of Fig. 5.

Light Absorption.—All the sols of actomyosin are characterised by a light-absorption maximum at 275 mμ, in agreement with previous observations relating to the protein which had not been in contact with ion-exchangers (Schauenstein and Treiber, *J. Polymer Sci.*, 1950, **5**, 145; Laki, Bowen, and Clark, *J. Gen. Physiol.*, 1949/50, **33**, 430). The band is due to electronic transitions, an effect which is assumed not to play a significant rôle at $\lambda > 350$ mμ. The assumption is justified by a consideration of the amino-acid composition of actomyosin (cf. Bailey, *loc. cit.*) in conjunction with empirically well-established relations between chemical structures and light absorption.

Viscosities.—The reciprocal observed viscosities of solutions of actomyosin, $1/\eta$, were plotted, at each concentration of the protein, against the rate of shear, γ, the graph thus obtained being

TABLE 7. *Range of protein concentration and rate of shear in which measurements for calculation of intrinsic viscosity of actomyosin sols were carried out; shear-rate dependence of viscosity.*

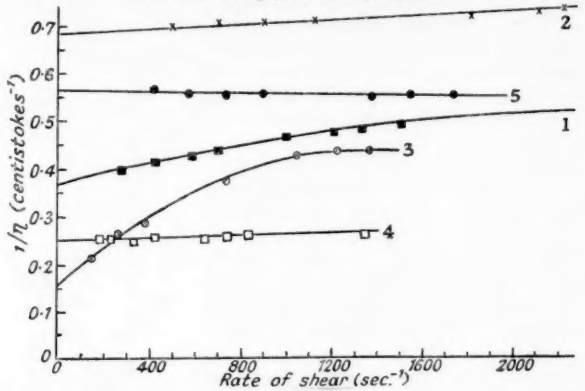
Treatment of actomyosin with ion exchanger	Solvent	pH	Ionic strength	Protein concentration, C (g./100 cm.³ of sol)	Rate of shear (sec.$^{-1}$)	$10^4\alpha$ (sec./centistoke) for C = 0·100 and 20·0°
—	Buffer *A*	6·46	0·537	0·0300—0·553	282—2708	
	Buffer *C*	8·26	0·540	0·0865—0·693	106—2708	
+	Buffer *A*	6·46	0·537	0·0580—0·279	501—2708	
	Buffer *E*	7·77	0·501	0·0433—0·173	50—2860	
	Buffer *D*	4·00	0·100	0·0470—0·284	464—2780	<1
	Soltn. of KCl	2·90	0·100	0·0800—0·640	406—2710	
	H_2O	2·50	—	0·0800—1·28	367—2710	
		3·50	—	0·0940—0·377	464—2760	
		4·00	—	0·0560—0·450	184—2592	
		4·26	—	0·0280—0·450	207—2680	
		6·50	—	0·0230—0·460	531—2860	3 ± 1
		7·20	—	0·0150—0·292	50—2860	>3
		8·20	—	0·0164—0·0655	148—2732	6 ± 2
		9·30	—	0·0160—0·262	188—2488	<1
		11·50	—	0·0608—0·288	403—2833	

For composition of buffers, see Tables 4—6 and legend to Fig. 1.

extrapolated to $\gamma \longrightarrow 0$, thereby estimating the relevant viscosity, η', at zero rate of shear. The reduced viscosities, $(\eta'/\eta_0 - 1)/c$ or $(\ln \eta'/\eta_0)/c$ (where η_0 is the viscosity of solvent), were plotted against c, the concentration of actomyosin, extrapolation to $c \longrightarrow 0$ enabling a comput-

ation of the intrinsic viscosity, $[\eta]$. Typical results of measurements showing the influence of γ and c are shown in Figs. 8 and 9, and the various values of $[\eta]$, together with a few reduced viscosities, are shown in Fig. 10. These $[\eta]$ values were calculated from measurements carried

FIG. 8. *Influence of rate of shear on viscosities of actomyosin sols; temp.*, 20·0°. *Protein concentrations, c, in g./100 cm.³ of solution.*



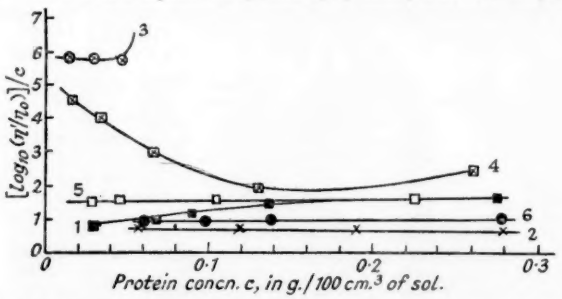
(1) Before treatment with ion-exchange resins; sol prepared from gel (I), solvent buffer *A* (Table 4), pH 6·46; $\mu = 0{\cdot}537$; $c = 0{\cdot}276$.
(2)—(5) After treatment with exchange resins.
(2) Sol (III) brought to pH 6·46 by addition of KOH; KCl and phosphates subsequently added. Solvent, pH and μ as in (1); $c = 0{\cdot}276$.
(3) Sol (III) brought to pH 7·20 by addition of KOH; no salt or buffer added; $c = 0{\cdot}0655$.
(4) Sol (III); pH 4·26; no salt or buffer added; $c = 0{\cdot}450$.
(5) Sol (III) brought to pH 11·5 by addition of KOH; no salt or buffer added; $c = 0{\cdot}288$.

out in the range of concentration and rates of shear given in cols. 5 and 6 of Table 7; the last column of the Table contains the value of the quantity defined by

$$\alpha = [\mathrm{d}(1/\eta)/\mathrm{d}\gamma]_{\gamma \to 0} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

which was estimated from the initial slope of such graphs as those shown in Fig. 8. If solutions of actomyosin of pH 11·5 or <4·0 are treated with appropriate ion-exchange resins, or if the

FIG. 9. *Concentration dependence of viscosity of actomyosin sols; temp.*, 20·0°.



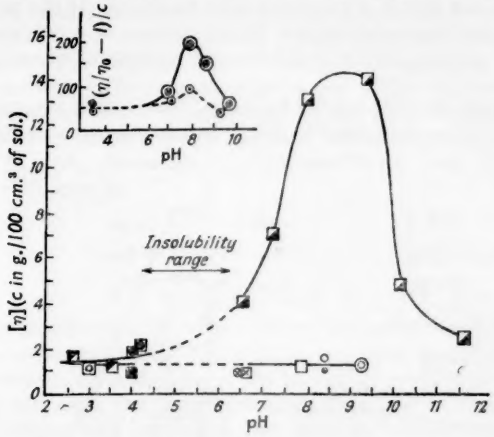
η' = viscosity of solution, extrapolated to zero rate of shear; η_0 = viscosity of solvent.
(1) Before treatment with ion-exchange resins. Solvent buffer *A* (Table 4); pH 6·46; $\mu = 0{\cdot}537$.
(2)—(6) After treatment with ion-exchange resins.
(2) Solvent, pH, and μ as in (1); (3) pH 7·20; (4) pH 9·30; (5) pH 4·26; (6) pH 11·5. In (3)—(6) the solvent was water, no salts or buffers being added.

required quantity of potassium hydroxide is added, the pH can be brought back to the range 6·5—9·0. The $[\eta]$ values of these latter sols were not significantly different from those of sols whose pH had not been above 8·5 or below 4·0.

Reaction of Actomyosin with Ion-exchange Resins.—These do not substantially alter the weight-average molecular weight, M, or the intrinsic viscosity, $[\eta]$, of the protein (as shown by ref. nos.

1, 2, 6, and 7 of Table 6 and by the experiments at pH 6·46 and $\mu = 0{\cdot}539$, represented in Fig. 10), the electrometric titration curve, the pH of the " intersection point " shown in Fig. 2, or the electrophoretic migration velocity. The concentration dependence of the reduced turbidities (curves *a* and *b* in Fig. 5) and the flow birefringence in 0·5M-potassium chloride decrease on treatment with the resins, while the solubility in water increases.

FIG. 10. *Influence of* pH *on intrinsic viscosities of actomyosin sols; temp.* 20·0°.



Symbol ..... ⊗ ⊠ ○ ● □ ■ ◎ ⊡ ◩ ⊛ ◪ (pH 6·5—10) ◪ pH (11·5)

Accuracy of $[\eta]$ ..... ± 0·1—0·2 ± 1—2 ± 0·2

⊗ and ○ Actomyosin not treated with exchange resins; all other symbols relate to actomyosin after treatment with resins.

⊗ and ⊠ Solvent buffer *A* (Table 4); $\mu = 0{\cdot}537$.
○ and ● Solvent buffer *C* (Table 5); $\mu = 0{\cdot}540$.
□ Solvent = solution of KCl; $\mu = 0{\cdot}500$; K–veronal buffer; $\mu = 0{\cdot}013$.
■ Solvent buffer *D* (Table 6); $\mu = 0{\cdot}100$.
◎ Solvent = solution of KCl, $\mu = 0{\cdot}600$; K_2CO_3, $\mu = 0{\cdot}030$; $KHCO_3$, $\mu = 0{\cdot}040$ (buffer *E*).
⊡ Solvent = solution of KCl; $\mu = 0{\cdot}100$.
◩ No salts or buffer added, pH adjusted by addition of HCl to sol (III).
⊛ Sol (III) without addition of salts or buffers.
◪ No salts or buffers added; pH adjusted by addition of KOH to sol (III).

Inset: Influence of pH *on reduced viscosities of actomyosin sols; temp.*, 0°.

No salts or buffer added; pH adjusted by addition of KOH or HCl to sol (III); protein concentration, *c*, in g./100 cm.^{3} of solution.

⊗ $c = 0{\cdot}105$; rates of shear 194—719 sec.$^{-1}$.
◉ $c = 0{\cdot}0525$; rates of shear 576—857 sec.$^{-1}$.

DISCUSSION

Possibility of Polymerisation Reactions.—The actomyosin sols can be divided into groups: (*a*) solvent water, pH 8·0 and 9·5, (*b*) solvent 0·5—0·6M-potassium chloride, pH 7·8, 8·3, and 9·2; (*c*) solvent water, pH 11·5; (*d*) pH <5. It will be seen from Figs. 8, 9, and 10 that the intrinsic viscosities, $[\eta]$, of sols (*a*) are 13 ± 2 and 14 ± 2, while those of sols (*b*) and (*c*) are between 0·8 and 2·5, the influence of rate of shear and of protein concentration being relatively small in the last case. If actomyosin, in dilute solution, were taken to be a rigid structure, stabilised by hydrogen bonds or salt bridges,* an interpretation of the change of properties on passing from sols (*a*) to (*b*) and (*c*) could be attempted, by assuming the occurrence of a reversible polymerisation reaction, the $[\eta]$ value of polymerised actomyosin being large. The protein being represented by an

* The salt bridge of actomyosin, not treated with ion-exchange resins, may be due to, *inter alia*, polyfunctional ionic impurities.

ellipsoid of rotation, of partial specific volume 0·75, and solvation being neglected, it follows from Simha's formula (*J. Phys. Chem.*, 1940, **44**, 25; cf. also Kuhn, Kuhn, and Buchner, *Ergebn. exakt. Naturwiss.*, 1951, **25**, 39) that the axial ratio of the proteins in sols (*a*) and (*b*) is respectively 175 and 37; if end-to-end alignment of the ellipsoids occurred, the molecular weight of the solute in sols (*a*) should be about 470% larger than that of the actomyosin in sols (*b*). The experimentally determined molecular weights (ref. nos. 6—9, Table 6) show that the difference, if any, is at the most 60%, and it is concluded that the high intrinsic viscosity of sols (*a*) is not due to a polymerisation reaction. If the protein is represented by a cylindrical rod, the argument against the occurrence of a polymerisation reaction is similar (for reference relating to the hydrodynamic treatment of rods, see Kuhn, Kuhn, and Buchner, *loc. cit.*).

Qualitative Interpretation of Results of Viscosity Tests.—It is assumed that actomyosin, in dilute solution, is composed of flexible chains which take up an extended configuration

FIG. 11.

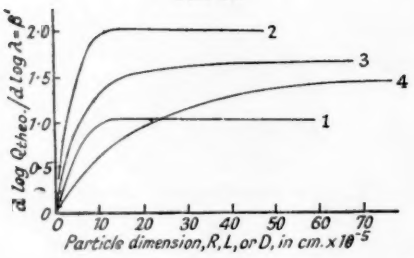


FIG. 12.

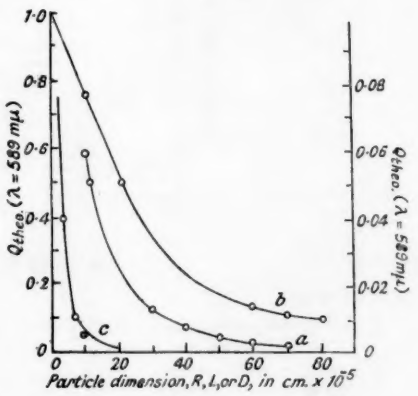


FIG. 11.

d log $Q_{theor.}$/d log $\lambda = \beta'$ (see equation 6) plotted against particle dimensions.
D = diameter of sphere; R = root-mean-square distance between ends of coiled chain; L = length of thin rod.
(1) Thin rod. (2) Sphere. (3) Monodisperse coil. (4) Polydisperse coil. The analytical expressions for (1)—(3) are given by Bueche, Debye, and Cashin (*loc. cit.*); the expression for (4) is due to Doty and Steiner (*loc. cit.*).

FIG. 12.

$Q_{theor.}$ for $\lambda = 589$ mμ, on ordinate, plotted against particle dimension, D or R on abscissa; D = diameter of sphere; R = root-mean-square distance between ends of coiled chains.
(*a*) = Monodisperse coil, relates to right-hand ordinate; (*b*) = polydisperse coil, and (*c*) = sphere, both relate to left-hand ordinate. In all three cases $Q_{theor.}$ decreases on passing on abscissa from left to right.

if side-chain groupings repel each other, owing to a negative electrostatic charge. Such effects are made responsible for the high $[\eta]$ values of sols (*a*), but it is not to be supposed that the pH of maximum intrinsic viscosity coincides with the equivalent point (cf. Fuoss, *Discuss. Faraday Soc.*, 1951, **11**, 125). On addition of salts, buffer, or excess of potassium hydroxide, an increased binding of counter ions will take place, thereby decreasing the net charge on the protein and reducing the electrostatic repulsion. This screening of the charge must lead to more compact chain configuration, possibly of higher statistical probability, and therefore the $[\eta]$ values of sols (*b*) and (*c*) are small. It follows from (15) (below) that a decrease of $[\eta]$ from 13·5 to 1·4 corresponds to a contraction of the protein chain of about 100%.

Some previously investigated proteins (for references, see Pauli and Valko, "Elektrochemie der Kolloide," Vienna, 1929, chapter 44) or synthetic polyampholytes (Alfrey, Fuoss, and Morawetz, *J. Amer. Chem. Soc.*, 1952, **74**, 438) are characterised by viscosity

maxima on each side of the isoelectric point. In the case of actomyosin a second maximum has not been observed, the $[\eta]$ values of sols (*d*) being small compared with those of sols (*a*). This can be explained by assuming that the binding of chloride counter-ions by positively charged actomyosin ions is sufficiently large, even in the absence of added potassium chloride, to prevent a significant electrostatic repulsion of the side-chain groupings of the proteins, and an increase of the average distance between the chain ends. The bonds between counter-ions and actomyosin ion, $I^{m(+)}$ or $I^{m(-)}$, will be partly ionic and partly covalent in character, like simple salt links (cf., *e.g.*, Bell and Prue, *J.*, 1949, **362**, where references to previous work will be found); and disperion forces, depending on the polarisability of the counter-ions and of the side-chain groupings of the protein, have also to be taken into account. The relative importance of the various contributions is not known, but the binding of simple counter-ions by the ions of natural or synthetic polyelectrolytes, $P^{q(-)}$, is well established (Scatchard, Scheinberg, and Armstrong, *J. Amer. Chem. Soc.*, 1950, **72**, 533; Huizenga, Grieger, and Wall, *ibid.*, 1950, **72**, 4228). It is possible that such equilibria as

$$n\mathrm{Cl}^{(-)} + \mathrm{I}^{m(+)} \rightleftharpoons \mathrm{I}^{m(+)} \ldots . n\mathrm{Cl}^{(-)} \quad . . . . . \quad (9)$$

$$m\mathrm{K}^{(+)} + \mathrm{I}^{m(-)} \rightleftharpoons \mathrm{I}^{m(-)} \ldots . m\mathrm{K}^{(+)} \quad . . . . . \quad (10)$$

$$q\mathrm{K}^{(+)} + \mathrm{P}^{q(-)} \rightleftharpoons \mathrm{P}^{q(-)} \ldots . q\mathrm{K}^{(+)} \quad . . . . . \quad (11)$$

are characterised by constants of greatly different numerical values and it would not be justified, therefore, to postulate that electrostatic screening by counter-ions and viscosity properties must be similar on both sides of the isoelectric point of actomyosin.

Fuoss (*loc. cit.*) discussed the concentration dependence of the reduced viscosity of synthetic polyelectrolytes and explained the typical "concave-up" shape frequently observed. Graphs (**3**) and (**4**) in Fig. 9 are of a different shape, which may be due to stronger binding of counter-ions by the actomyosin, corresponding to a marked difference in the position of equilibria (**10**) and (**11**).

Order of Magnitude of Molecular Dimensions.—Numerical values of β', defined by (**6**), for various dimensions of scattering particles are shown by the graphs in Fig. 11. It will be seen that the limiting values, β'_∞, relating to sufficiently large solute molecules are respectively 2·0, 1·7, 1·45, and 1·0 for spheres, monodisperse coiled chains, polydisperse coiled chains, and thin rods. The experimentally determined β values, $1{\cdot}7 \pm 0{\cdot}3$ (mean of figures in col. 9 of Table 6), are not compatible with β'_∞ (rod) and can only be reconciled with graphs 2, 3, or 4 of Fig. 11 if D (diameter) $> 8 \times 10^{-5}$ cm. for spheres, R (root-mean-square distance between ends of coiled chain) $> 15 \times 10^{-5}$ cm. for monodisperse coils, or $R > 40 \times 10^{-5}$ cm. for polydisperse coils. $Q_{\text{theor.}}$ decreases with increasing size of the solute, as shown, for a specified wave-length, in Fig. 12, and therefore the lower limits of D and R require upper limits for $Q_{\text{theor.}}$. These upper limits ($\lambda = 589$ mμ) are as follows:

$$Q_{\text{theor.}} < 0{\cdot}08 \text{ (sphere)} \quad . . . . . \quad (12)$$

$$Q_{\text{theor.}} < 0{\cdot}03 \text{ (monodisperse coil)} \quad . . . . . \quad (13)$$

$$Q_{\text{theor.}} < 0{\cdot}25 \text{ (polydisperse coil)} \quad . . . . . \quad (14)$$

$Q_{\text{exp.}}$ ($\lambda = 589$ mμ) is $0{\cdot}14 \pm 0{\cdot}04$ (mean of figures in last column of Table 6); this value cannot be reconciled with (**12**) or (**13**) but is compatible with (**14**), and it follows that the sphere and monodisperse coil models are also ruled out. Comparison of $Q_{\text{exp.}}$ with graph (*b*) in Fig. 12 shows that the root-mean-square end-to-end distance, R, of actomyosin, represented as a polydisperse coil, is $(60 \pm 10) \times 10^{-5}$ cm. The accuracy of these R values is not sufficient to distinguish between extended and contracted protein molecules. Under the conditions of these experiments, length changes of about 100% appear to occur (cf. above) but these are not sufficient to bring about a transition from a coiled chain to a rod-like configuration.

It appears of interest to estimate the R values of these actomyosin preparations with the help of a different method, involving the use of the following relation.

$$R = \{[\eta]M\}^{\frac{1}{3}} \times B \quad . . . . . \quad (15)$$

where $[\eta]$ is the intrinsic viscosity, in terms of g. of solute per 100 cm.^{3} solution, M is the molecular weight of the solute, and B is a constant. This formula applies to flexible chains like macromolecules; it is not suggested, however, that in the present case the hydrodynamic thickness of the solute is of low molecular dimensions. If one assumes that the chain molecule is sufficiently long, it can be shown (cf. Kuhn, Kuhn, and Buchner, *loc. cit.*, p. 103) that the numerical values of the constant are as follows: $B = 7{\cdot}3 \times 10^{-8}$ (Kuhn, Moning, and Kuhn, *Helv. Chim. Acta*, 1953, **36**, 747), $B = 6{\cdot}5 \times 10^{-8}$ (Kirkwood and Riseman, *J. Chem. Physics*, 1948, **16**, 573; 1949, **17**, 442; Wilson, *ibid.*, p. 217), $B = 7{\cdot}8 \times 10^{-8}$ (Flory and Fox, *J. Polymer Sci.*, 1950, **5**, 745). On introduction in (15) of $7{\cdot}2 \times 10^{-8}$ for B, 2×10^8 for M (see col. 8, Table 6), and 13·5 (sols *a*) and 1·4 (sols *b*) for $[\eta]$, it follows that R is respectively 10×10^{-5} and 5×10^{-5} cm. These values are smaller than the dimension estimated from light scattering but of the same order of magnitude.

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William Ramsay and Ralph Forster Laboratories,
University College, London. [*Received, October 7th*, 1953.]

The Action of Perphthalic Acid on 5-Dihydroergosteryl and Ergosteryl Acetates.

By G. H. Alt and D. H. R. Barton.

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Treatment of 5-dihydroergosteryl acetate with perphthalic acid gives the corresponding 7 : 8-epoxide. Under controlled acid conditions the latter affords a mixture of ergosta-7 : 9 (11) : 22- and -7 : 14 : 22-trien-3β-yl acetates as well as a minor proportion of 7-oxoergost-22-en-3β-yl acetate.

Similar treatment of ergosteryl acetate affords a complex mixture, in which 3β-acetoxyergosta-7 : 22-diene-5α : 6β-diol has been identified. Evidence for the presence of the 6-(hydrogen phthalate) of this compound and of its 6-epimer has been adduced. Two other compounds of unknown structure have also been isolated.

The constitution of the minor yeast sterol, cerevisterol, has been elucidated as ergosta-7 : 22-diene-3β : 5α : 6β-triol.

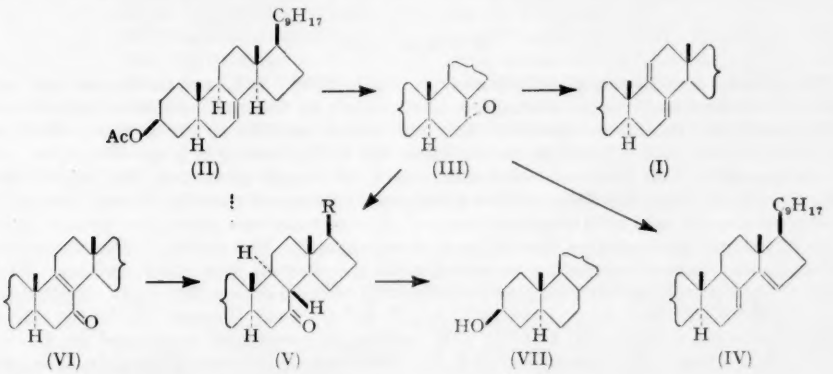
The conjugated diene 3β-acetoxyergosta-7 : 9(11) : 22-triene (ergosterol D acetate; Barton, *J.*, 1946, 512) (I) has become an important intermediate in potential cortisone syntheses (see Birch, *Ann. Reports*, 1951, 204; Cornforth, *ibid.*, 1952, 190). This compound is most efficiently prepared by dehydrogenation of 5-dihydroergosteryl acetate (II) with bromine or chlorine (Anderson, Budziarek, Newbold, Stevenson, and Spring, *Chem. and Ind.*, 1951, 1035 and subsequent papers) or with mercuric acetate (Windaus and Auhagen, *Annalen*, 1929, **472**, 185; Heilbron, Johnstone, and Spring, *J.*, 1929, 2248; see also Anderson *et al.*, *loc. cit.*). Dehydrogenation with selenium dioxide has also been reported (Callow and Rosenheim, *J.*, 1933, 387). We now describe an alternative route for the conversion of (II) into (I) (cf. Windaus and Lüttringhaus, *Annalen*, 1930, **481**, 119).

Treatment of (II) with one molecular proportion of perphthalic acid in ether gave the monoepoxide (III).* The α-configuration of the epoxide ring is based on the concept of preferred attack from the α-side of the molecule (Fieser, *Experientia*, 1950, **6**, 312; Gallagher and Kritchevsky, *J. Amer. Chem. Soc.*, 1950, **72**, 882). An alternative allylic

* The compound to which this structure was previously assigned (see Callow and Rosenheim, *loc. cit.*) has subsequently been shown by Fieser and Ourisson (*J. Amer. Chem. Soc.*, 1953, **75**, 4404) to be otherwise constituted.

alcohol formulation for (III) is excluded by its resistance to acetylation and by the absence of a hydroxyl band in the infra-red spectrum. Controlled acid-catalysed dehydration of (III) in aqueous dioxan afforded, as main product, a mixture of dienes. Treatment of this mixture with maleic anhydride in benzene solution gave, as the more insoluble product, the maleic anhydride adduct of ergosta-7 : 14 : 22-trien-3β-yl acetate (IV), whilst the more soluble product was identified as ergosta-7 : 9(11) : 22-trien-3β-yl acetate (I). The rotation of the diene mixture indicated that it contained 60% of the desired (I) and 40% of (IV). This was confirmed (*a*) by quantitative experiments with maleic anhydride (" dienometry ") as detailed in the Experimental section and (*b*) by the preparation of an artificial mixture of the dienes which had the same m. p., mixed m. p., and (by design) rotation.

The minor product of the acid-catalysed dehydration of (III) was identified as 7-oxoergost-22-en-3β-yl acetate (V; R = C_9H_{17}). An authentic specimen of this compound was prepared from 7-oxoergosta-8 : 22-dien-3β-yl acetate (VI) (Heusser, Eichenberger, Kurath, Dällenbach and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106) by lithium and liquid ammonia reduction followed by reacetylation. The stability of this compound to attempted base-catalysed inversion of configuration at $C_{(8)}$ was demonstrated. Palladium-catalysed hydrogenation afforded 7-oxoergostan-3β-yl acetate (V; R = C_9H_{19}) which on Wolff–Kishner reduction gave ergostanol (VII; R = C_9H_{19}). The correctness of the α-configuration at $C_{(9)}$ in (V; R = C_9H_{17} and C_9H_{19}) is thus confirmed. The molecular rotations observed for (V; R = C_9H_{17}) and (V; R = C_9H_{19}) were −301° and −211° respectively. These are in good agreement with those calculated (−308° and −206° respectively) from standard data (Barton and Cox, *J.*, 1948, 1354; Barton, Cox, and Holness, *J.*, 1949, 1771; Barton and Klyne, *Chem. and Ind.*, 1948, 755).



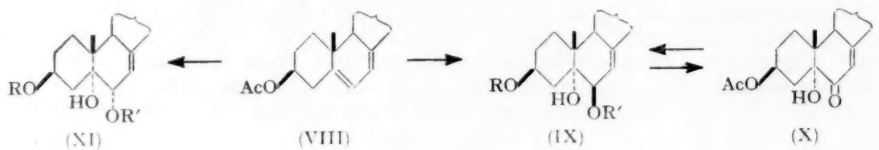
A complementary study of the action of perphthalic acid in ethereal solution on ergosteryl acetate (VIII) has also been undertaken. After separation of acid reaction products (hydrogen phthalates : see below) the neutral reaction products were chromatographed to give three compounds : $C_{30}H_{48}O_4$, $C_{30}H_{46}O_4$, and a conjugated diene $C_{30}H_{46}O_3$. The constitutions of the last-mentioned substances have not been elucidated with certainty, but the first has been identified as 3β-acetoxyergosta-7 : 22-diene-5α : 6β-diol (IX; R = Ac, R′ = H) on the basis of the following evidence. Mild acetylation furnished a diacetate (IX; R = R′ = Ac); similar benzoylation conditions gave an acetate benzoate (IX; R = Ac, R′ = Bz); alkaline hydrolysis afforded a triol (IX; R = R′ = H), converted into the diacetate on acetylation. Chromic acid oxidation gave 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (X) (Burawoy, *J.*, 1937, 409) from which (IX; R = R′ = H) was re-formed on lithium aluminium hydride reduction.* The assignment of

* Professors L. F. Fieser (Harvard) and C. W. Shoppee (Swansea) have very kindly informed us that they have also effected this reduction to (IX : R = R′ = H) : see Mary Fieser, Quilico, Nickon, Rosen, Tarlton, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4066; Blears and Shoppee, *Chem. and Ind.*, 1953, 947.

the 6β-configuration in (IX) was based, in our preliminary communication (Alt and Barton, *Chem. and Ind.*, 1952, 1103), on molecular-rotation arguments. These need not be repeated here, since compelling, and superior, chemical evidence for the correctness of this conclusion has recently been adduced by Fieser *et al.* (*loc. cit.*).

From the acid fraction (see above), after hydrolysis and reacetylation, a mixture of (IX; R = R′ = Ac) (30%) and of its 6-epimer (XI; R = R′ = Ac) (70%) was isolated. Since derivatives of (IX) do not isomerise to derivatives of (XI) under conditions at least as drastic as those involved in the perphthalic acid oxidation and subsequent processing, we conclude that (IX) and (XI) are initially present as the 6-(hydrogen phthalates) of (IX; R = Ac, R′ = H) and of (XI; R = Ac, R′ = H).

One of the minor yeast sterols, cerevisterol, $C_{28}H_{46}O_3$, was isolated and characterised as the diacetate by Honeywell and Bills (*J. Biol. Chem.*, 1932, **99**, 71; 1933, **103**, 515). It has also been obtained from *Amanita phalloides* and from ergot (Wieland and Coutelle, *Annalen*, 1941, **548**, 270). We noted a correspondence in properties between cerevisterol and its diacetate and (IX; R = R′ = H) and its diacetate. Through the courtesy of Dr. C. E. Bills, to whom we express our best thanks, it was possible to make a direct comparison and thus to confirm these identities. The constitution of cerevisterol as (IX; R = R′ = H) may therefore be taken as established (Alt and Barton, *loc. cit.*).



(XI) (VIII) (IX) (X)

Experimental

For general experimental details see *J.*, 1952, 2339. $[\alpha]_D$ are in chloroform unless stated otherwise; ultra-violet absorption spectra are in ethanol. Infra-red spectra were kindly determined in carbon disulphide solution, unless specified to the contrary, by Messrs. Glaxo Laboratories Ltd. Light petroleum refers to that fraction of b. p. 40—60°.

7-Oxoergost-22-en-3β-yl Acetate.—7-Oxoergosta-8 : 22-dien-3β-yl acetate (400 mg.) (Heusser *et al.*, *loc. cit.*) in dry ether (40 ml.) was added to a solution of metallic lithium (200 mg.) in liquid ammonia (40 ml.) with vigorous stirring. The mixture was stirred for 30 min. and the excess of lithium destroyed by the addition of *n*-propanol. The product, after reacetylation (400 mg.), was chromatographed over alumina (12 g.; washed with ethyl acetate). Elution with 9 : 1 light petroleum–benzene gave *7-oxoergost-22-en-3β-yl acetate* (300 mg.). Recrystallised from methanol this had m. p. 185—187°, $[\alpha]_D$ −66° (*c*, 1·02) (Found: C, 78·95; H, 10·4. $C_{30}H_{48}O_3$ required C, 78·9; H, 10·6%). The acetate was recovered unchanged (m. p., mixed m. p., and rotation) after hydrolysis with 3% methanolic potassium hydroxide under reflux for 1 hr. followed by re-acetylation (pyridine–acetic anhydride overnight at room temperature).

7-Oxoergostan-3β-yl Acetate.—The unsaturated ketone (100 mg.) in ethyl acetate (20 ml.) was hydrogenated with a palladised calcium carbonate catalyst (5%; 100 mg.) for 4 hr., to give *7-oxoergostan-3β-yl acetate*, m. p. 178—180° (from methanol), $[\alpha]_D$ −46° (*c*, 1·10) (Found: C, 78·95; H, 10·9. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). The ketone (65 mg.) in ethanol (2·5 ml.) was heated with a solution of sodium (200 mg.) in ethanol (3 ml.) and hydrazine hydrate (1 ml.) at 200° for 14 hr. Crystallisation from methanol afforded ergostan-3β-ol, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ + 15° (*c*, 1·24)}.

7α : 8α-Epoxyergost-22-en-3β-yl Acetate.—5-Dihydroergosteryl acetate (880 mg.) was treated with perphthalic acid (9 mg./ml.: 2 mols.) in ethereal solution at room temperature for 5 days (consumption of 1 mol. of per-acid). The product {800 mg.; m. p. 140—146°, $[\alpha]_D$ −14° (*c*, 1·32)} in light petroleum solution was filtered through alumina (ethyl acetate-washed). Crystallisation from light petroleum gave *7α : 8α-epoxyergost-22-en-3β-yl acetate* (200 mg.). This had m. p. 161—163°, $[\alpha]_D$ −19° (*c*, 1·32), and no ketonic absorption in the ultra-violet (Found: C, 78·7; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). It was recovered unchanged on attempted acetylation (pyridine–acetic anhydride at room temperature). Further elution of the alumina column with light petroleum afforded a small amount of a *compound*,

m. p. (from light petroleum) 190—192°, $[\alpha]_D$ −30° (*c*, 1·07) (Found: C, 76·0; H, 10·2. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%), which is probably the 7 : 8-22 : 23-diepoxide.

Treatment of 7α : 8α-Epoxyergost-22-en-3β-yl Acetate with Acid.—The oxide (4·0 g.) in dioxan (200 ml.; redistilled over sodium) and aqueous 2N-sulphuric acid (10 ml.) was left at room temperature for 48 hr. (no further increase in the intensity of the ultra-violet absorption spectrum). The product (4·0 g.), which had $\lambda_{max.}$ 236 and 243 mμ (ε 9200 and 10,200 respectively), in ethanol (150 ml.) was refluxed with semicarbazide hydrochloride (1·2 g.) and anhydrous sodium acetate (1·0 g.) for 20 min. The total product in benzene solution (50 ml.) was filtered through alumina (100 g.). Elution with benzene (100 ml.) and 19 : 1 benzene–ether gave a product (3·6 g.) which was crystallised from chloroform–methanol, to furnish a diene mixture (2·0 g.), m. p. 155—160°, $[\alpha]_D$ −70° (*c*, 1·80), $\lambda_{max.}$ 236 and 243 mμ (ε 11,800 and 13,000 respectively). Elution of the column with ether–methanol, hydrolysis with 5N-ethanolic sulphuric acid at room temperature for 24 hr., and re-acetylation (pyridine–acetic anhydride) gave a product which was chromatographed over alumina (34 g.). Elution with mixtures of light petroleum and benzene gave diene mixtures (200 mg.). Elution with 4 : 1 benzene–ether afforded fractions (200 mg.), which on crystallisation from methanol gave 7-oxoergost-22-en-3β-yl acetate, identified by m. p., mixed m. p., and rotation.

The diene mixture of $[\alpha]_D$ −70° (see above)(100 mg.) in dry benzene (5 ml.) was refluxed with maleic anhydride (15 mg.; redistilled) for 4 hr. Preliminary experiments showed that this time of reflux was adequate for the quantitive conversion of ergosta-7 : 14 : 22-trien-3β-yl acetate into its maleic anhydride adduct. The benzene was removed *in vacuo* and the residue extracted with light petroleum. Evaporation of the light petroleum and crystallisation from chloroform–methanol furnished ergosta-7 : 9(11) : 22-trien-3β-yl acetate (50 mg.), m. p. 172—174°, $[\alpha]_D$ +29° (*c*, 1·34), $\lambda_{max.}$ 236 and 242 mμ (ε 15,300 and 17,000 respectively), undepressed in m. p. on admixture with an authentic specimen of the same physical constants. The residue from the extraction with light petroleum was recrystallised from benzene, to give ergosta-7 : 14 : 22-trien-3β-yl acetate–maleic anhydride adduct, m. p. 197—203°, undepressed in m. p. on admixture with an authentic specimen of the same m. p. range.

To confirm that the diene mixture consisted solely of ergosta-7 : 9(11) : 22- and -7 : 14 : 22-trien-3β-yl acetates, the rotation of the diene mixture before and after refluxing with maleic anhydride was determined and the resultant rotational shift was compared with that which would be expected on the basis that the diene mixture was a two-component system of composition determined by its initial rotation. All rotatons were taken in benzene. The pure compounds had: ergosta-7 : 9(11) : 22-trien-3β-yl acetate, $[\alpha]_D$ +23° (*c*, 2·08); ergosta-7 : 14 : 22-trien-3β-yl acetate, $[\alpha]_D$ −212° (*c*, 1·12); derived maleic anhydride adduct, $[\alpha]_D$ −96° (*c*, 0·77). The results obtained, shown in the Table, indicate that the diene mixture

	Control mixture of ergosta-7 : 9(11) : 22- (56·5%) and -7 : 14 : 22-(43·5%)-trien-3β-yl acetates		Mixture of dienes. Calc. by assuming ergosta-7 : 9(11) : 22- (60%) and -7 : 14 : 22 (40%) -trien-3β-yl acetates	
	Obsd.	Calc. from known composition of mixture	Obsd.	Calc. on above assumption
$[\alpha]_D$ (in C_6H_6) of mixture	−78° (*c*, 3·20)	−79°	−68° (*c*, 3·26)	−71°
$[\alpha]_D$ (in C_6H_6) after refluxing with 2·5 mols. of maleic anhydride	−35° (*c*, 1·92)	−37°	−33° (*c*, 1·96)	−33°

consisted of 60% of ergosta-7 : 9(11) : 22-trien-3β-yl acetate and 40% of the 7 : 14 : 22-isomer (the validity of the method is shown by the results given in the Table for the artificial 56·5 : 43·5 mixture made up from pure components). This was confirmed by the preparation of an artificial mixture of the two acetates in these proportions which had m. p. 155—160°, $[\alpha]_D$ −69° (*c*, 1·47), and gave no depression in m. p. on admixture with the diene mixture of $[\alpha]_D$ −70°.

Treatment of Ergosteryl Acetate with Perphthalic Acid.—Ergosteryl acetate (8·8 g.) was treated with perphthalic acid (25 mg./ml.; 3 mols.) in ether at 0° for 18 hr. (uptake of 1·5 mols.). The solution was washed with 5% aqueous sodium hydroxide and water. Removal of the ether *in vacuo* and azeotropic drying with benzene furnished a solid (5·5 g.), m. p. 150—170°, $\lambda_{max.}$ 253 mμ (ε 4000). This was dissolved in benzene (150 ml.) and filtered through alumina (120 g.; ethyl acetate-washed). Elution with benzene gave material (2·4 g.) of m. p. 165—185°. Elution with 1 : 1 benzene–ether afforded material (2·5 g.), m. p. 253—257°, which, on

crystallisation from chloroform–methanol, furnished 3β-*acetoxyergosta*-7 : 22-*diene*-5α : 6β-*diol*, m. p. 255—258°, $[\alpha]_D$ −52° (*c*, 1·09) (Found : C, 75·25; H, 10·15. $C_{30}H_{48}O_4,\frac{1}{2}CH_3{\cdot}OH$ requires C, 74·95; H, 10·3%), giving a pale yellow colour with tetranitromethane. Acetylation with pyridine–acetic anhydride overnight at room temperature gave the *diacetate*, m. p. 168—170° (from ethanol), $[\alpha]_D$ −149° (*c*, 1·58) (Found : C, 74·25; H, 9·65. $C_{32}H_{50}O_5$ requires C, 74·65; H, 9·8%), undepressed in m. p. on admixture with authentic cerevisterol diacetate of m. p. 169—171°, $[\alpha]_D$ −143° (*c*, 1·07). Hydrolysis of the monoacetate (150 mg.) with methanolic potassium hydroxide (5%; 10 ml.) gave ergosta-7 : 22-diene-3β : 5α : 6β-triol. Recrystallised from ethyl acetate this had m. p. 253—256°, $[\alpha]_D$ −84° (*c*, 1·39 in pyridine), undepressed in m. p. on admixture with an authentic specimen of cerevisterol, m. p. 256—259°, $[\alpha]_D$ −83° (*c*, 0·89 in pyridine); reacetylation gave the diacetate mentioned above (m. p. and mixed m. p.).

Treatment of the monoacetate (100 mg.) with pyridine–benzoyl chloride overnight at room temperature gave 3β-*acetoxy*-6β-*benzoyloxyergosta*-7 : 22-*dien*-5α-*ol*, m. p. 179—182° (from ether–methanol), $[\alpha]_D$ −156° (*c*, 0·84) (Found : C, 77·4; H, 9·2. $C_{37}H_{52}O_5$ requires C, 77·05; H, 9·1%), depressed in m. p. on admixture with an authentic specimen of 3β-acetoxy-6α-benzoyloxyergosta-7 : 22-dien-5α-ol, m. p. 186—187°, $[\alpha]_D$ +44° (*c*, 1·14), prepared by the method of Windaus and Lüttringhaus (*loc. cit.*).

The monoacetate (100 mg.) in "AnalaR" acetic acid (5 ml.) was treated with chromium trioxide (17 mg.; 1·2 mols.) in the minimum of water and left overnight at room temperature. Recrystallisation of the product from ethyl acetate furnished 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one, m. p. 262—264°, $[\alpha]_D$ −4° (*c*, 1·46), $\lambda_{max.}$ 250 mμ (ε 13,500), undepressed in m. p. on admixture with an authentic specimen (Burawoy, *J.*, 1937, 409) of the same m. p. and rotation. This ketone (200 mg.) was extracted from the thimble of a Soxhlet extractor into a solution of lithium aluminium hydride (100 mg.) in dry ether (50 ml.). Working up in the usual way and crystallisation from ethyl acetate furnished ergosta-7 : 22-diene-3β : 5α : 6β-triol, m. p. and mixed m. p. 253—256°, $[\alpha]_D$ −83° (*c*, 1·19 in pyridine).

The material (2·4 g.), m. p. 165—185°, mentioned above was rechromatographed over alumina (60 g.; ethyl acetate-washed). Elution with light petroleum afforded a *compound* (1·5 g.) which, after recrystallisation from ethyl acetate–methanol, had m. p. 209—212°, $[\alpha]_D$ −103° (*c*, 1·94), no selective absorption in the range 220—320 mμ (Found : C, 76·85; H, 9·75. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85%).

Elution with 1 : 1 light petroleum–benzene furnished a further *compound* (250 mg.) which, recrystallised from methanol, had m. p. 126—128°, $[\alpha]_D$ +33° (*c*, 1·65 in CCl_4), $\lambda_{max.}$ 253 mμ (ε 25,500) (Found : C, 79·3; H, 10·3. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). This substance deteriorates rapidly to a yellow gum and is also very sensitive to acid. To show that it was not an αβ-unsaturated ketone the compound (70 mg.) in dry ether (50 ml). was refluxed with lithium aluminium hydride (70 mg.) for 24 hr. Working up, reacetylation (pyridine–acetic anhydride at room temperature overnight), and crystallisation from ethyl acetate–methanol gave back starting material, identified by m. p., mixed m. p., rotation, and absorption spectrum.

Examination of the Sodium Hydroxide Wash-liquors.—The 5% sodium hydroxide wash-liquors (see above; from a preparation starting with 2·2 g. of ergosteryl acetate) were acidified with aqueous hydrochloric acid and extracted with ether. The product was refluxed with 5% methanolic potassium hydroxide (100 ml.) for 1 hr. Crystallisation of the hydrolysate from ethanol gave a product (800 mg.), m. p. 235—237°, $[\alpha]_D$ −6° (*c*, 1·10 in pyridine). This was acetylated (pyridine–acetic anhydride overnight at room temperature) and chromatographed over alumina (15 g.; ethyl acetate-washed). Elution with light petroleum and mixtures therewith containing up to 50% of benzene gave 3β : 6α-diacetoxyergosta-7 : 22-dien-5α-ol, m. p. (from ethanol) 178—180°, $[\alpha]_D$ +34° (*c*, 2·24), undepressed in m. p. on admixture with an authentic specimen of m. p. 179—181°, $[\alpha]_D$ +38° (*c*, 1·15), prepared according to the method of Windaus and Lüttringhaus (*loc. cit.*). Elution with benzene gave 3β : 6β-diacetoxyergosta-7 : 22-dien-5α-ol, m. p. (from ethanol) 168—170°, $[\alpha]_D$ −146° (*c*, 1·11), undepressed in m. p. on admixture with an authentic specimen (see above).

The assumption that the material of m. p. 235—237°, $[\alpha]_D$ −6° (see above), was a mixture of ergosta-7 : 22-diene 3β : 5α : 6β- and 3β : 5α : 6α-triol showed from the rotation that it must be of the composition 30 : 70. An authentic mixture of these proportions had, after crystallisation, m. p. and mixed m. p. 235—237°.

Attempted Epimerisation of 6β-*Compounds.*—3β-Acetoxyergosta-7 : 22-diene-5α : 6β-diol (53 mg.) in chloroform (5 ml.) underwent no change during 2 days at room temperature or 1 hr. under reflux. Similarly the corresponding 6β-benzoate was unchanged in refluxing chloroform solution (2 hr.) with or without the addition of benzoic acid (2 mols.). The 3-acetate 6β-benzoate

(10 mg.) was also unchanged when left in chloroform (3 ml.) solution containing toluene-*p*-sulphonic acid (0·6 mg.) at room temperature for 3 days.

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The Structure of the Oligosaccharides produced by the Enzymic Breakdown of Pectic Acid. Part I.

By J. K. N. JONES and W. W. REID.

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Pectic acid is degraded by the enzymes of *Aspergillus fœtidus*, Thom and Raper, with the formation of D-galacturonic acid, digalacturonic acid, and trigalacturonic acid. Constitutional studies on the trisaccharide and the disaccharide are described. A summary of part of the work now described has appeared earlier (Jones and Reid, *Chem. and Ind.*, 1953, 303).

PECTIC ACID is believed to be composed of a large number of D-galactopyruronic acid residues, linked together by α-glycosidic linkages, with the resultant formation of a linear polysaccharide of high molecular weight (cf. Hirst and Jones, *Adv. Carbohydrate Chem.*, 1946, **2**, 235, for a review).

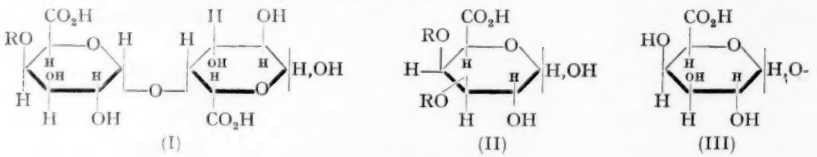
It is well known that pectic acid is rapidly degraded by enzymes which are produced by certain varieties of fungi. One of us (W. W. R.) has observed that *Aspergillus fœtidus*, Thom and Raper, under defined cultural conditions produces a (D)-type enzyme which degrades pectic acid to a mixture of D-galacturonic acid and two oligosaccharides only (Ayres, Dingle, Phipps, Reid, and Solomons, *Nature*, 1952, **170**, 834). From the mixture, by fractional precipitation, it is possible to obtain pure samples of a disaccharide and a trisaccharide. The efficiency of the fractionation of these galacturonic acid derivatives was followed on paper chromatograms. The di- and the tri-saccharide were purified as the calcium salts; that of the trisaccharide was difficult to obtain in a crystalline form. It was assumed that no resynthesis by enzymic action occurred during the formation of these oligosaccharides.

In order to determine the structure of the trisaccharide (I; R = III or II; R = III) the free acid was converted into the methyl glycoside of the methyl ester, the carbomethoxy-groups of which were then reduced in aqueous solution with sodium borohydride. The resulting galactose derivative was then methylated with sodium hydroxide and methyl sulphate, Purdie's reagents, and thallous ethoxide and methyl iodide, and the product was hydrolysed. There resulted a mixture of three sugars which were identified on paper chromatograms and separated cellulose (Hough, Jones, and Wadman, *J.*, 1949, 2511). The sugars were identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose, 2 : 3 : 6-tri-*O*-methyl-D-galactose and crystalline 2 : 6-di-*O*-methyl-D-galactose. The yields of sugars approximated to a ratio of 1 : 1·3 : 1. The isolation of these sugars suggests either (*a*) that the trisaccharide is of the unbranched-chain type (I; R = III), which on hydrolysis should yield one mole of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose and two moles of 2 : 3 : 6-tri-*O*-methyl-D-galactose, or (*b*) that the trisaccharide is of the branched-chain type (II; R = III), which should yield on hydrolysis two molecules of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose and one mole of di-*O*-methyl-D-galactose.

In either case the deviation of the ratios of the respective sugars from 1 to 2 and 2 to 1 may be due to incomplete methylation perhaps owing to formation of esters of boron acids (cf. experimental section) or perhaps to some steric factor. In view of the results of Hough, Jones, and Richards (*Chem. and Ind.*, 1953, **40**, 1064) further discussion is deferred until more information is available as to the effect of sodium borohydride on

oligosaccharides of this type. These reactions prove for the first time that some at least of the uronic acid residues in pectic acid are in the pyranose form. These results were reported in brief earlier (cf. Jones and Reid, *loc. cit.* *Note:* their formula I is incorrect).

Sufficient of the crystalline diuronide was available for its analysis, and the determination of its physical properties and rate of movement on the chromatogram. Since the isolation of this crystalline substance is a long and tedious procedure it was decided to convert apple pectic acid, by enzymic degradation with the (D)-type enzyme, into the resulting mixture of triuronide (60%), diuronide (20%), and galacturonic acid (20%), and then to fractionate this mixture after it had been converted into a mixture of methyl ester methyl glycosides. Accordingly the crude mixture of the calcium salts of these three galacturonic acid derivatives (Ayres *et al.*, *loc. cit.*) was shaken with cold methanolic hydrogen chloride until a sample no longer reduced Fehling's solution. The resulting methyl ester methyl glycosides were then fractionated on charcoal (Darco G 60) (Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677), and the syrupy uronides of lower molecular weight which were eluted with water were isolated and methylated first with sodium hydroxide and methyl sulphate and then with Purdie's reagents. The carbomethoxy-groups in the mixture of methylated galacturonic acid derivatives were then reduced with lithium aluminium hydride and the resultant mixture of methylated galactose-containing oligosaccharides was again methylated with Purdie's reagents. With this procedure no complications due to the formation of boron derivatives are possible and the methylated derivatives may be further fractionated by distillation. Fractional distillation of this product gave two main fractions and a still residue. The first fraction was identified after



(I) (II) (III)

hydrolysis as mainly **2 : 3 : 4 : 6**-tetra-*O*-methyl-D-galactose, and the second fraction, after hydrolysis and separation on cellulose, yielded a mixture of **2 : 3 : 4 : 6**-tetra-*O*-methyl-D-galactose, **2 : 3 : 6**-tri-*O*-methyl-D-galactose, and **2 : 3 : 4**-tri-*O*-methyl-D-galactose. The ratio of "tetra and **2 : 3 : 4**-tri" to "**2 : 3 : 6**-tri" was about **1 : 1**). Evidently some of the hydroxyl groupings on C_6 had escaped methylation. Accordingly the still residue (fraction 3) was remethylated and the product distilled and hydrolysed. Only two sugars resulted: **2 : 3 : 4 : 6**-tetra-*O*-methyl-D-galactose and **2 : 3 : 6**-tri-*O*-methyl-D-galactose. It is evident that the original product consisted of a D-galactopyranose residue linked to a second D-galactose residue through C_4 or C_5. The linkage joining the two sugar residues is very probably of the α-glycosidic type since it results from the reduction of a disaccharide with a high positive optical rotation (+160°).

It follows that there was present in the enzymic hydrolysate a disaccharide (I; R = H) composed of a D-galacturonic acid residue in the pyranose form, linked very probably by an α-link to a second D-galacturonic acid residue, and that the linkage was very probably through $C_{(4)}$ because the disaccharide possesses a high positive rotation.

Experimental

The following solvents were used in chromatographic separation on Whatman No. 1 paper: (*a*) ethyl acetate–acetic acid–formic acid–water (**18 : 3 : 1 : 4**); (*b*) *n*-butanol–pyridine–water (**10 : 3 : 3**); (*c*) *n*-butanol–ethanol–water (**40 : 11 : 19**); and (*d*) ethyl acetate–acetic acid–water (**3 : 1 : 3**) (top phase); all v/v. Ammoniacal silver nitrate (Partridge, *Biochem. J.*, 1948, **42**, 238) and *p*-anisidine hydrochloride solution were used as spray reagents to detect glycosides and reducing sugars, respectively. With solvent mixture (*d*), bromophenol blue (0·2% of the sodium salt in 50% v/v ethanol) was used to detect acids. Optical rotations were determined at 20° ± 2° in water, unless otherwise stated. Microanalyses are by Mr. B. S. Noyes of Bristol. Evaporation of solutions was carried out under reduced pressure.

By the action of a (D)-type enzyme preparation from *Aspergillus fœtidus*, Thom and

Raper, on apple pectic acid at pH 3·5 a mixture of mono-, di-, and tri-galacturonic acids was obtained (Ayres, Dingle, Phipps, Reid, and Solomons, *loc. cit.*). The calcium salts of these acids were repeatedly precipitated from 60% v/v ethanol in which the calcium salt of galacturonic acid is soluble. The calcium salts of the di- and tri-galacturonic acids, which were insoluble in 60% ethanol, were fractionated from aqueous solution with ethanol. The fractions from the lower ethanol concentrations were pure samples of the calcium trigalacturonate, and those from the higher alcohol concentrations were pure calcium digalacturonate. The intermediate fractions (about 80% of the starting material) were mixtures of the two compounds. The samples of the calcium salts of the di- and tri-galacturonic acids did not crystallise from water. An aqueous solution of each sample was therefore treated with ZeoCarb 225 to remove calcium ions. The filtrate and washings were then evaporated to dryness under reduced pressure, and the dry acid mixed with the equivalent amount of dry calcium carbonate. On the addition of a few drops of water, the mass dissolved with effervescence and in each case crystallised immediately. The crystalline calcium di- and tri-galacturonates so obtained, were used to inoculate aqueous solutions of the mixed calcium di- and tri-galacturonates. The mixtures were left to crystallise in desiccators over sulphuric acid; after 2—3 weeks a crystalline mush was formed in each case. The crystals were collected and washed with water. The nearly pure samples so obtained were suspended in water, and ZeoCarb 225 was added with stirring until the crystals had dissolved. The resin was filtered off and washed with water, and the filtrates and washings were neutralised with calcium carbonate, filtered, and concentrated. The thin syrups so obtained were inoculated with the appropriate seed crystals and left over sulphuric acid for 2—3 weeks to crystallise. The white crystalline mush was filtered off (sintered glass), washed with water, ethanol, and ether, and dried at room temperature. The crystalline calcium salts were chromatographically pure [solvent (*d*)]. In some experiments the calcium trigalacturonate set to a stiff gel. When this was ground in a mortar with water, an amorphous, chromatographically pure calcium salt was obtained. It was not soluble in water but dissolved readily in dilute mineral acids.

Trigalacturonic Acid.—The *calcium salt* crystallised from water as rosettes of minute needles, and was dried at room temperature. It had $[\alpha]_D$ +154° (*c* 1·44, in N-HCl) (Found: C, 29·5; H, 5·2; Ca, 8·35. $C_{18}H_{23}O_{19}1\frac{1}{2}Ca,7H_2O$ requires C, 29·6; H, 5·1; Ca, 8·2%). When dried to constant weight, the sample lost weight (Found: loss, 10·3. Calc. for $4H_2O$: loss, 9·7%). The residual *trihydrate* (Found: C, 33·3; H, 4·4. $C_{18}H_{23}O_{19}1\frac{1}{2}Ca,3H_2O$ requires C, 33·2; H, 4·3%) was hygroscopic. A sample of the calcium salt (equivalent to 1 mmol. of anhydrous trisaccharide) gave, on complete hydrolysis with an (S)-type pectic enzyme preparation (Ayres *et al.*, *loc. cit.*), only D-galacturonic acid which was detected on paper chromatograms [solvents (*c*) and (*d*)] (Found, by hypoiodite oxidation: 2·96 mmol.; galacturonic acid requires 3·00 mmol.).

The free *acid* (1·30 g.) was prepared from the calcium salt by deionisation with ZeoCarb 225 [Found: equiv., 191 (by titration); *M*, 557 (after oxidation with hypoiodite). $C_{18}H_{26}O_{19},H_2O$ requires equiv., 188; *M*, 564)]. The dried *acid* (1·23 g.) (Found: C, 39·6; H, 4·9. $C_{18}H_{26}O_{19}$ requires C, 39·5; H, 4·8%) was dissolved in dry methanolic hydrogen chloride (1·5% w/v; 100 c.c.), and the solution set aside in a stoppered vessel at room temperature until a sample no longer reduced Fehling's solution (24 hr.). The solution was then neutralised (Ag_2CO_3), filtered, and evaporated. The residual glassy solid (1·2 g.) was dissolved in water (50 c.c.), and reduced with sodium borohydride (0·4 g.). The solution was left for 7 days at room temperature, it was then acidified with acetic acid and filtered, and the filtrate deionised by a column of Amberlite resins IR120 and IR4B. The neutral effluent was concentrated to a solid (0·98 g.) which was dried by dissolution in methanol followed by removal of the solvent. It had $[\alpha]_D$ +190° (*c*, 9·8) (Found: OMe, 13·1. Calc. for $C_{19}H_{28}O_{19}$: OMe, 5·6%). The reason for this high methoxyl value is obscure but it may be due to contamination of the product with some non-reduced methyl ester of the trigalactosiduronic acid or with boric esters. A portion (0·89 g.) was methylated with sodium hydroxide and methyl sulphate (twice), silver oxide and methyl iodide, thallium ethoxide and methyl iodide, and finally with silver oxide and methyl iodide. The product (0·73 g.) (Found: OMe, 46·3. Calc. for $C_{29}H_{54}O_{16}$: OMe, 52·1%) was a thick yellow syrup which could not be distilled without decomposition. A portion (0·69 g.) was hydrolysed with boiling N-hydrochloric acid (10 c.c.) for 8 hr. ($[\alpha]_D$ +190° ⟶ +101°, constant value). The cooled solution was neutralised (Ag_2CO_3) and filtered before and after the passage of hydrogen sulphide, and the filtrate concentrated to a syrup (0·65 g.). Paper-chromatographic examination of a portion of the syrup [solvent (*b*)] indicated the presence of three sugars with R_G * 0·93, 0·84, and 0·64, in approximately equal proportions. The syrup

* R_G is the rate of movement relative to tetra-*O*-methylglucopyranose.

was fractionated on cellulose, the top layer of benzene–ethanol–water (34 : 10 : 3 v/v) being used as mobile phase. Concentration of the appropriate fractions of the effluent from the column gave: Fraction **1** (0·166 g.), $[\alpha]_D$ +104° (*c*, 1·4), identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose by its rate of movement on the chromatogram [solvents (*a*), (*b*), and (*c*)] and characterised as the *N*-phenylgalactosylamine, m. p. and mixed m. p. with an authentic specimen 194°. Fraction 2 (0·219 g.), $[\alpha]_D$ +89° (*c*, 3·6) (Found: OMe, 42·1. Calc. for $C_9H_{18}O_6$: OMe, 41·9%), moved at the same rate as 2 : 3 : 6-tri-*O*-methyl-D-galactose on the chromatogram [solvents (*a*), (*b*), and (*c*)] and after oxidation with bromine water under the usual conditions yielded 2 : 3 : 6-tri-*O*-methyl-D-galactofuranolactone, m. p. 99° not depressed in admixture with an authentic specimen (Found: OMe, 40·4. Calc. for $C_9H_{16}O_6$: OMe, 42·3%). Fraction 3 (0·19 g.), $[\alpha]_D$ +82° (*c*, 3·8), slowly crystallised. The substance was recrystallised from acetone–ether–light petroleum (b. p. 40—60°) and then had m. p. 131°, not depressed on admixture with an authentic specimen of 2 : 6-di-*O*-methyl-D-galactose (Found: C, 46·1; H, 7·5; OMe, 31·3. Calc. for $C_8H_{16}O_6$: C, 46·1; H, 7·7; OMe, 29·8%). After the crystals had been kept in air, the m. p. fell, owing to formation of a hydrate of 2 : 6-di-*O*-methyl-D-galactose.

Digalacturonic Acid.—(*a*) A small amount of the *calcium salt* of the disaccharide was crystallised from water and dried over calcium chloride; the sheaves of needles had $[\alpha]_D$ +119° (*c*, 1·30 in N-HCl) (Found: C, 29·4; H, 5·3; Ca, 8·1. $C_{12}H_{16}O_{13}Ca,5H_2O$ requires C, 29·0; H, 5·2; Ca, 8·2%). When dried the pentahydrate lost weight (Found: loss, 13·1. Calc. for $4H_2O$: loss, 14·4%). The residual *monohydrate* (Found: C, 33·8; H, 4·9. $C_{12}H_{16}O_{13}Ca,H_2O$ requires C, 33·4; H, 4·2%) was extremely hygroscopic. Part of the crystalline calcium salt was converted into the free acid with ZeoCarb 225 and concentrated to a glassy solid (Found: equiv., by titration, 202; *M*, after oxidation with hypoiodite, 390. $C_{12}H_{18}O_{13},H_2O$ requires equiv., 199; *M*, 398). A sample of the calcium salt (equivalent to 1 mmole of anhydrous disaccharide) gave, on complete hydrolysis with an (S)-type pectic enzyme preparation (Ayres *et al.*, *loc. cit.*), D-galacturonic acid only, detected on paper chromatograms [solvents (*c*) and (*d*)] (Found: by hypoiodite oxidation, 2·02 mmole. Required, galacturonic acid, 2·00 mmole). The oxidation of a sample of this material with bromine water gave inconclusive results; similarly its reduction with sodium borohydride or sodium amalgam did not give a crystalline product.

(*b*) A mixture of oligosaccharides obtained by the action of a (D)-type pectic enzyme [from *Aspergillus fœtidus*, Thom and Raper, (Ayres *et al. loc. cit.*)] on apple pectic acid was used as starting material. Chromatographic examination [solvent (*a*)] of this material showed that it contained D-galacturonic acid, much di- and tri-saccharides, and traces of oligosaccharides of high molecular weight. The rates of movement relative to galactose in solvent (*a*) were galacturonic acid, 0·96 (weak); disaccharide, 0·29 (strong), 0·18 (faint); trisaccharide, 0·12 (very strong).

The crude mixture of calcium salts (20 g.) was shaken with methanolic hydrogen chloride (2% w/v; 250 c.c.); much dissolved rapidly, and after 48 hr. at 20° the solution was non-reducing. Hydrogen chloride was removed by addition of silver carbonate, and the solution was filtered and concentrated to a syrup (14 g.). Chromatographic examination [solvent (*b*)] on paper showed at least seven components moving at the following rates [relative to rhamnose (1·0)]: 1·7, 1·5, 1·0, 0·7, 0·55, 0·35, and 0·08. The picture had been complicated by the formation of the glycoside anomers. Accordingly the syrup was fractionated on Celite–charcoal (22 × 5 cm. diam.) (Whistler and Durso, *loc. cit.*). Elution with water and concentration of the effluent gave a syrup (9·1 g.) which contained five components [solvent (*b*)] whose rate of movement relative to rhamnose was 0·7, 0·55, 0·4, 0·16, and 0·18, the second and the third component predominating. The mixture of non-reducing glycosides was methylated with sodium hydroxide (30%) and methyl sulphate six times, by the usual procedure; the reaction mixture was concentrated between each operation. The solution was then acidified with sulphuric acid and extracted exhaustively with chloroform. Concentration of the extract gave a syrup (5 g.) (Found: OMe, 25·0%), which was again methylated with Purdie's reagents, and the product (4·18 g.), n_D^{20} 1·4780, $[\alpha]_D$ +120° (*c*, 1·8 in MeOH) (Found: OMe, 47·1%), was reduced with lithium aluminium hydride in dry ether. Excess of lithium aluminium hydride was destroyed by water, the slurry of aluminium hydroxide, ether, and water was filtered, the residue was well washed with water, and the filtrate was concentrated to dryness. Extraction of the residue with chloroform gave a syrupy galactose derivative (3·08 g., from 3·4 g. of galacturonic acid derivative). This product was again methylated with Purdie's reagents (yield 2·76 g.) and then distilled *in vacuo* giving: fraction 1 (0·4 g.), b. p. 120°/0·5 mm., n_D^{20} 1·4482 (Found: OMe,

59·7%); fraction 2 (0·17 g.), b. p. 120—150°/0·5 mm., n_D^{20} 1·4518 (Found: OMe, 57·6%); fraction 3 (0·91 g.), b. p. 225—240°/0·5 mm., n_D^{19} 1·4740 (Found: OMe, 50·0%); and a residue (1·3 g.) (Found: OMe, 41·3%).

Fractions 1 and 2 were combined and hydrolysed with boiling N-sulphuric acid. Chromatographic examination [solvent (*b*)] indicated that 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose was the major component, together with some 2 : 3 : 5 : 6-tetra-*O*-methyl-D-galactose and traces of trimethyl-D-galactose. The sugars were isolated in the usual way and heated with a solution of aniline in ethanol whereupon 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-galactosylamine, m. p. and mixed m. p. 194°, was produced.

Fraction 3 (0·88 g.) was hydrolysed with boiling N-hydrochloric acid (25 c.c.) for 6 hr. The optical rotation was not observable owing to the darkening of the solution. The solution was neutralised by addition of silver carbonate and filtered before and after the passage of hydrogen sulphide. Concentration of the filtrate gave a syrup (0·8 g.), $[\alpha]_D$ +89° (*c*, 2·5), examination of which on the paper chromatogram showed presence of three components [R_G 0·93, 0·83, and 0·77, in solvent (*c*)]; the first two gave a red colour with the *p*-anisidine hydrochloride spray, the third a brown colour. The syrup was fractionated on cellulose, benzene–ethanol (19 : 1 v/v) being used as eluent. By concentration of the appropriate portion of the effluent three main fractions were obtained and were identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (0·29 g.), $[\alpha]_D$ +107° (*c*, 5·0) [the *N*-phenylgalactosylamine derivative had m. p. 193°]; 2 : 3 : 6-tri-*O*-methyl-D-galactose (0·203 g.), $[\alpha]_D$ +57° ⟶ +90° (*c*, 3·3 in water) (2 : 3 : 6-tri-*O*-methyl-D-galactofuranolactone, m. p. and mixed m. p. 90°); and 2 : 3 : 4-tri-*O*-methyl-D-galactose (0·10 g.), m. p. (hydrate) 80°, $[\alpha]_D$ +113° (*c*, 1·7) (the *N*-phenyl-D-galactosylamine derivative had m. p. 169°, not depressed in admixture with an authentic specimen). The rates of movement of these sugars on paper chromatograms were not distinguishable from those of authentic specimens. After separation of these sugars, the cellulose column was eluted with alcohol. Concentration of the solvent left a syrupy mixture of di-*O*-methylgalactoses (0·04 g.).

The still residue (1·3 g.) was dissolved in water and methylated three times with 30% sodium hydroxide and methyl sulphate and the product isolated by chloroform extraction. Concentration of the extract gave a syrup (0·81 g.) which was again methylated (Purdie's reagents) and distilled. The product (0·75 g.) had b. p. 210°/0·3 mm., $[\alpha]_D$ +150° ± 20° (*c*, 0·12, in MeOH) (micropolarimeter tube) (Found: OMe, 54·4. Calc. for $C_{20}H_{38}O_{11}$: OMe, 54·6%). This product was hydrolysed with boiling N-hydrochloric acid for 6 hr., and the methylated sugars isolated in the usual way. Chromatographic analysis of the syrup (0·71 g.) indicated that it contained two sugars only. These were separated on cellulose, benzene–ethanol (19 : 1 v/v) being used as mobile phase, and were identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (0·33 g.), $[\alpha]_D$ +112° (*c*, 3·3) (Found: OMe, 52·0. Calc. for $C_{10}H_{20}O_6$: OMe, 52·5%) (the *N*-phenylgalactosylamine derivative had m. p. 194°, not depressed on admixture with an authentic specimen), and 2 : 3 : 6-tri-*O*-methyl-D-galactose (0·3 g.), $[\alpha]_D$ +88° equilibrium (*c*, 3·0) (Found: OMe, 42·0. Calc. for $C_9H_{18}O_6$: OMe, 41·9%), which was identified after oxidation with bromine water as 2 : 3 : 6-tri-*O*-methyl-D-galactofuranolactone, m. p. 96° not depressed on admixture with an authentic specimen.

CHEMISTRY DEPARTMENT, BRISTOL UNIVERSITY.
RESEARCH DEPARTMENT, H. W. CARTER & CO., LTD., COLEFORD, GLOUCESTERSHIRE.
[Present address (J. K. N. J.): QUEEN'S UNIVERSITY, KINGSTON, ONTARIO, CANADA.]

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Some Reactions of Optically Active 1-*Phenylpent*-1-*en*-3-*ol and* 1-*Phenylpent*-2-*en*-1-*ol.*

By M. P. Balfe, J. Kenyon, and D. Y. Waddan.

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The dibromo-alcohols formed by addition of bromine to optically active 1-phenylpent-1-en-3-ol yield, on oxidation, optically active 1 : 2-dibromo-1-phenylpentan-3-ones. These reactions are analogous to those observed by Kenyon and Partridge (*J.*, 1936, 1313) with (+)-4-phenylbut-3-en-2-ol. Evidence is now obtained that *both* the 1- and the 2-carbon atom contribute to the optical activity of the dibromo-alcohols and dibromo-ketones derived from the alkenols.

(+)- and (−)-1-Phenylpent-2-en-1-ols rearrange with complete racemisation to 1-phenylpent-1-en-3-ol, and a similar rearrangement of the hydrogen phthalates occurs with extensive, but incomplete, racemisation.

(+)- and (−)-1-Phenylpent-1-en-3-ol and (+)- and (−)-1-phenylpent-2-en-1-ol are readily obtained by the usual method of fractional crystallisation of alkaloidal salts of their hydrogen phthalates: details are given in the experimental section and rotatory data in Tables 1 and 2.

Table 1. *Specific rotatory Powers of* (+)-1-*ethyl*-3-*phenylprop*-2-*enyl* (1-*phenylpent*-1-*en*-3-*yl*) *hydrogen phthalate in various solvents at room temperature* (1, 2).

Solv.	c	$[\alpha]_{5893}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$	Solv.	c	$[\alpha]_{5893}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$
CS_2	1·40	+53·4°	+80·5°	+127°	Me_2CO	2·02	−6·2°	− 9·1°	−13·1°
AcOH	2·27	26·1	32·1	63·5	Et_2O	2·00	−7·8	− 9·0	−13·9
C_5H_5N	1·61	17·0	19·8	38·2	EtOH	13·85	−4·4	− 5·0	− 7·2
CCl_4	2·16	11·5	14·3	30·4			(−)-isomeride		
$CHCl_3$	2·38	9·4	12·2	26·2					
C_6H_6	2·32	+7·3	+11·4	+20·6	$CHCl_3$	1·60	−9·5°	−12·0°	−26·7°

Table 2. *Specific rotatory powers in the homogeneous state.*

(*a*) 1-*Phenylpent*-1-*en*-3-*ol* (d_4^{20} 0·9980)

	l	t	$[\alpha]_{5893}$	$[\alpha]_{5780}$	$[\alpha]_{5461}$	$[\alpha]_{5036}$	$[\alpha]_{4800}$	$[\alpha]_{4358}$
(+)-Alcohol	0·5	21°	+6·7°	+7·2	+8·4°	+10·9°	+13·4°	+19·8°
(−)-Alcohol	0·5	21°	−6·7	−7·3	−8·3	−10·8	−13·4	−19·6

(*b*) 1-*Phenylpent*-2-*en*-1-*ol* (d_4^{25} 0·9894)

(−)-Alcohol	0·5	19°	−12·6	−13·0	−14·8	−19·8	−20·9	−26·0

From the evidence given later it seems probable that 1-phenylpent-1-en-3-ol in both its racemic and optically active forms has been obtained exclusively in the *trans*-modification.

A mixture of two stereoisomeric forms of 1 : 2-dibromo-1-phenylpentan-3-ol, m. p. 93—94° and m. p. 114—115°, in 60% and 40% yields, respectively, is obtained by the addition of bromine at room temperature to (+)-, (−)-, or (±)-1-phenylpent-1-en-3-ol. Oxidation of the resultant dibromo-alcohols gives 1 : 2-dibromo-1-phenylpentan-3-one, m. p. 109—110°, in about 90% yield. This single chemical species of dibromo-ketone is formed on oxidation of any of the stereoisomeric dibromo-alcohols, but it is produced as the (+)- or (−)- or (±)-variety according to which optical species of dibromo-alcohol has undergone oxidation. Somewhat unusually, the optically active and optically inactive forms of the dibromo-alcohols have the same m. p. : this is true also of the dibromo-ketones. Rotatory powers are given in Table 3.

Since the formations of the dibromo-alcohols and dibromo-ketones are practically quantitative and since the two dibromo-ketones [the (+)- and the (−)-form] obtained from any one alcohol are homogeneous—for exhaustive fractional crystallisation of each effects no separation—it is improbable that a mixture of *cis*- and *trans*-dibromo-alcohols is formed by the addition of bromine to 2-phenylpent-1-en-3-ol; it is, in fact, currently

accepted that such a reaction yields only the *trans*-dibromide. The reaction scheme is given in Table 4.

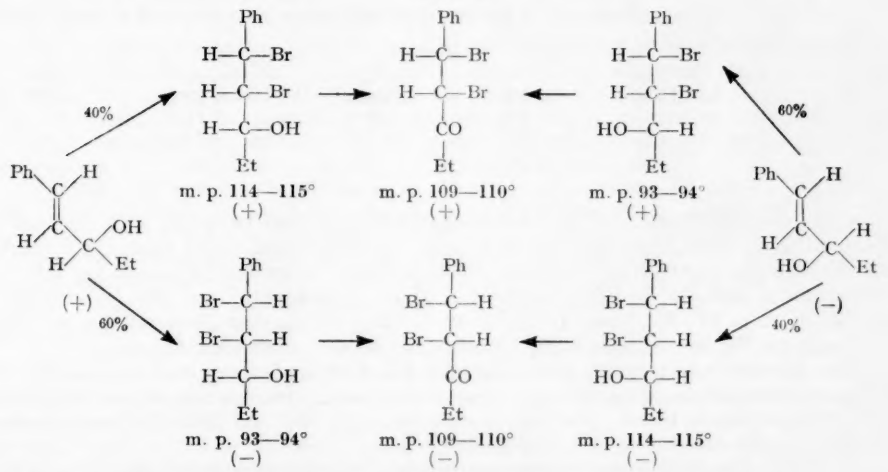
The two forms of the dibromo-alcohol are therefore diastereoisomerides, that of m. p. 114—115° containing a centre (or centres) of optical activity at $C_{(1)}$ or $C_{(2)}$ which has the

TABLE 3. *Specific rotatory powers of the dibromo-alcohols and dibromo-ketones* (in $CHCl_3$; *l*, 2).

	M. p.	*c*	$[\alpha]_{5893}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$
(+)-1 : 2-Dibromo-1-phenylpentan-3-ol	114—115°	1·47	+107·7°	+128·1°	+239°
(−)- ,, ,, ...	93—94	2·01	−106·9	−130·8	—
(−)- ,, ,, ...	114—115	1·72	−104·4	−125·3	−241
(+)- ,, ,, ...	93—94	2·03	+104·4	+129·5	+236
(+)-1 : 2-Dibromo-1-phenylpentan-3-one ...	109—110	1·71	+ 25·4	+ 30·1	+ 41
(−)- ,, ,, ,, ...	109—110	2·05	− 25·8	− 30·6	− 40

same sign of rotatory power as the original centre of optical activity—namely $C_{(3)}$; while that of m. p. 93—94° has a contribution of rotatory power from $C_{(1)}$ or $C_{(2)}$ which is opposite in sign to that of the original centre at $C_{(3)}$. From the (±)-alcohol the isomeric dibromo-alcohols are formed in the same proportions as from the (+)- and the (−)-alcohol but each is racemic, being formed in equal proportions from (+)- and (−)-optical species in the

TABLE 4.



(±)-alcohol. Although Kenyon and Partridge (*J.*, 1936, 1313) showed that 3 : 4-dibromo-4-phenylbutan-2-one obtained from (+)-4-phenylbut-3-en-2-ol is optically active they did not establish whether the optical activity is derived from $C_{(1)}$ or $C_{(2)}$ or from both $C_{(1)}$ and $C_{(2)}$. From the following considerations it is evident that both the $C_{(2)}$ and $C_{(3)}$ atoms in substituted allyl alcohols can become seats of optical activity when the 2 : 3-double bond becomes saturated: (−)-pent-1-en-3-ol yields, by similar reactions to those now described, (−)-1 : 2-dibromopentan-3-one (Partridge, Thesis, London, 1936) in which $C_{(2)}$ is the only possible seat of optical activity; whilst the rearrangement of the hydrogen phthalate of (−)-1-phenylbut-2-en-1-ol to that of (+)-1-phenylbut-1-en-3-ol (Kenyon, Partridge, and Phillips, *J.*, 1937, 207) similarly demonstrates that optical activity can arise when $C_{(3)}$ becomes asymmetrically saturated.

(+)-Et·CH(OH)·CH:CH_2 ⟶ Et·CH(OH)·CHBr·CH_2Br ⟶ (−)-Et·CO·CHBr·CH_2Br

(−)-Me·CH:CH·CHPh ⟶ (+)-Me·CH·CH:CHPh

O·CO·C_6H_4·CO_2H O·CO·C_6H_4·CO_2H

The experiments now described afford evidence that *both* carbon atoms become optically active when an optically active 1 : 3-disubstituted allyl alcohol combines with bromine; this evidence being the homogeneity of the derived dibromo-ketone. The ketone contains two asymmetric carbon atoms, at least one of which is optically active in the ketones derived from the (+)- or (−)-alcohol. If the second asymmetric carbon atom were not giving rise to optical activity, *i.e.* were present in its (+)-form in half the ketone molecules and in its (−)-form in the other half, the ketone would be a mixture of diastereoisomerides which could be separated by fractional crystallisation. Since such a separation cannot be effected it follows that the second carbon atom of the $C_{(2)}$—$C_{(3)}$ pair in the (+)- or (−)-dibromo-ketone is also optically active and both must therefore have become optically active during the combination of the unsaturated alcohol with bromine.

The course of the addition of bromine to 1-phenylpent-1-en-3-ol, like that to 1-phenylbut-1-en-2-ol (Kenyon and Partridge, *loc. cit.*), is sensitive to temperature. The mixture of dibromo-ketones obtained (by subsequent oxidation) when the (+)-alcohol combines with bromine at −10° has −9·0°; when combination takes place at +60° the rotatory power of the mixed ketones falls to zero and at intermediate temperatures the rotatory power becomes lower as the temperature of reaction rises.

The lack of rotatory power in the mixture of dibromo-ketones obtained *via* combination at 60° (cf. Table 5) cannot be due to the racemisation of an initially active dibromo-alcohol

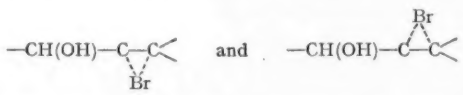
TABLE 5. *Specific rotatory powers of the* 1 : 2-*dibromo*-1-*phenylpentan*-3-*ones obtained by oxidation of the unseparated* 1 : 2-*dibromo*-1-*phenylpentan*-3-*ols prepared at temperature* t° (in $CHCl_3$; *l*, 2).

t	Medium	*c*	$[\alpha]_{5893}$	$[\alpha]_{5461}$	$[\alpha]_{4358}$
−10°	$CHCl_3$	1·55	−8·34°	−10·30°	−16·7°
+ 5	,,	2·90	5·20	6·11	8·4
22	,,	2·01	4·91	5·84	7·7
60	CCl_4	1·95	0	0	0
72	,,	1·80	0	0	0

since the dibromo-alcohol (of $[\alpha]_D$ −3·89° in chloroform) was recovered with unchanged rotatory power after its solution in chloroform has been heated under reflux for 2 hours; furthermore the (±)-mixture of dibromo-alcohols formed from the (+)-alcohol at 60° can be separated into the (+)-dibromo-alcohol of m. p. 114—115° and the (−)-dibromo-alcohol of m. p. 93—94° [these two dibromo-alcohols are diastereoisomerides, containing a (+)-centre of optical activity at $C_{(3)}$ and either a (+)- or (−)-centre at $C_{(1)}$—$C_{(2)}$].

The differences in rotatory power between the dibromo-ketones derived from the dibromo-alcohols produced at different temperatures must therefore be due to variations in the proportions of the two dibromo-alcohols (m. p. 93—94° and 114—115°, respectively) formed on addition of bromine to the alcohol.

It would appear that the equilibrium between the two stereoisomerides of the intermediate in the addition of bromine to the alcohol, which may be written :



is dependent on the temperature at which combination with bromine occurs : this equilibrium controls the relative proportions in which the diastereoisomeric dibromo-alcohols are formed when addition of the second atom of bromine ensues.

1-Phenylpent-2-en-1-ol rearranges very easily in the presence of acid to 1-phenylpent-1-en-3-ol. The (+)- and the (−)-alcohol, after some 3 days, yield products of changed sign of rotation which contain no optically active species of the original alcohol and yield the racemic diphenylylurethane and dibromo-derivatives of 1-phenylpent-1-en-3-ol. It therefore appears that the rearrangement occurs with complete racemisation, and that there is a concomitant formation of an optically active unidentified substance (or substances) in

small amount (see below). The alcohol also rearranges with complete racemisation on reaction with diphenylyl *iso*cyanate or pyridine hydrogen bromide perbromide in acetic acid solution forming the (±)-urethane of 1-phenylpent-1-en-3-ol and the acetate of (±)-1 : 2-dibromo-1-phenylpentan-3-ol, respectively: the racemisations do not occur after the formation of these derivatives, which are themselves optically stable under the conditions of the experiment. 1-Phenylpent-1-en-3-ol does not rearrange in the presence of acid, but undergoes mutarotation, probably due to the formation of an unidentified optically active substance, the alcohol recovered after the racemisation being substantially racemic.

The hydrogen phthalate of 1-phenylpent-2-en-1-ol rearranges very readily to that of 1-phenylpent-1-en-3-ol; if, during the preparation, the temperature exceeds 40°, only the rearranged product can be isolated. The homogeneous hydrogen phthalate racemises more rapidly than it rearranges and the product of rearrangement is the hydrogen phthalate of 1-phenylpent-1-en-3-ol possessing 39% of the maximum optical rotatory power. In solution (+)- or the (−)-1-phenylpent-2-en-1-yl hydrogen phthalate rearranges to the (−)- or the (+)-ester of 1-phenylpent-1-en-3-ol with varying degrees of racemisation according to the nature of the solvent. These rearrangements of 1-phenylpent-2-en-1-ol and its esters are analogous to those of 1-phenylbut-2-en-1-ol and its ester, which have been discussed by Kenyon, Partridge, and Phillips (*loc. cit.*), by Catchpole, Hughes, and Ingold (*J.*, 1948, 8), and by Braude *et al.* (*J.*, 1946, 396; 1947, 1096; 1948, 1982).

Experimental

(+)-1-Phenylpent-1-en-3-ol (126 g.), prepared by the addition of an ethereal solution of cinnamaldehyde (125 g.) to the Grignard reagent obtained from magnesium (24 g.) and ethyl chloride (68 g.), had b. p. 104—108°/2·5 mm. and n_D^{25} 1·5548 (cf. Levene and Stevens, *J. Biol. Chem.*, 1930, **87**, 375). An attempt to separate the alcohol into *cis*- and *trans*-isomerides by fractional distillation was unsuccessful. Its *p-diphenylylurethane* separates from benzene in needles, m. p. 150—151° (Found: N, 4·1. $C_{24}H_{23}O_2N$ requires N, 3·9%).

(±)-1-*Ethyl*-3-*phenylprop*-2-*enyl Hydrogen Phthalate*.—A mixture of the (±)-1-phenylpent-1-en-3-ol (162 g.), phthalic anhydride (148 g.), and pyridine (100 g.), heated for 1·5 hr. on the steam-bath, became a homogeneous, viscous liquid. Next day the product was diluted with ether and decomposed with dilute hydrochloric acid; the washed and dried (Na_2SO_4) solution, after dilution with light petroleum, deposited the *hydrogen phthalate* (284 g.) in irregular, glassy, rhombs (likewise from carbon disulphide), m. p. 109—110° (Found, by titration: *M*, 311. $C_{19}H_{18}O_4$ requires *M*, 310).

(+)-1-*Ethyl*-3-*phenylprop*-2-*enyl Hydrogen Phthalate*.—Cinchonidine (114 g.) was dissolved in a solution of the (±)-hydrogen phthalate (120 g.) in hot ethyl acetate (350 c.c.). After cooling, the *cinchonidine salt* of (+)-1-ethyl-3-phenylprop-2-enyl hydrogen phthalate separated and, after one recrystallisation from ethyl acetate, was obtained optically pure as bulky fibrous needles (96·5 g.), m. p. 175° (decomp.), $[\alpha]_{5893}$ −52·6°, $[\alpha]_{5461}$ −62·5°, $[\alpha]_{4358}$ −106° (*c*, 2·580 in $CHCl_3$; *l*, 2). On decomposition, by being covered with acetone and treated with dilute hydrochloric acid, it yielded the (−)-hydrogen phthalate as prismatic needles from carbon disulphide–light petroleum; it had m. p. 83—84° (decomp.). Rotatory powers are in Table 1.

(−)-1-*Ethyl*-3-*phenylprop*-2-*enyl Hydrogen Phthalate*.—The first filtrate from the crystallisation of the cinchonidine salt yielded a hydrogen phthalate (45·5 g.), with $[\alpha]_D$ −40·5° (in CS_2). To a portion (4·9 g.) of this in methyl acetate (15 c.c.) was added brucine (6·3 g.); the crystals, which slowly separated, after one recrystallisation from methyl acetate yielded optically pure *brucine salt* of the (−)-hydrogen phthalate; this formed needles, m. p. 118° (decomp.) $[\alpha]_{5983}$ −32·1°, $[\alpha]_{5461}$ −40·5°, $[\alpha]_{4358}$ −88° (*c*, 2·380 in $CHCl_3$; *l*, 2). The brucine salt (3·5 g.) when decomposed with acid yielded optically pure (−)-hydrogen phthalate (1·31 g.) as prismatic needles (from carbon disulphide–petroleum), m. p. 84° (decomp.).

Alternatively, and more conveniently, the optically impure (−)-hydrogen phthalate, by fractional crystallisation from carbon disulphide, yielded the optically pure ester, m. p. 83—84° (decomp.). Rotatory powers are in Table 1.

(+)-1-*Phenylpent*-1-*en*-3-*ol*—Sodium hydroxide (5N; 50 c.c.) was added to a solution of the (+)-hydrogen phthalate (30 g.) in ethanol (100 c.c.), the whole heated on the steam-bath for 1 hr. and then in a current of steam. The steam-distillate yielded the (+)-alcohol (14 g.), b. p. 110—112°/2·5 mm., n_D^{25} 1·5549, d_4^{25} 0·9980: rotatory powers are in Table 2. Its p-*diphenyl*-

ylurethane separates from benzene in bulky fine needles, m. p. 163—164° (Found: N, 4·2%), $[\alpha]_{5893}$ +144°, $[\alpha]_{5461}$ +180°, $[\alpha]_{4358}$ +402° (*c*, 0·671 in $CHCl_3$; *l*, 2).

(−)-1-Phenylpent-1-en-3-ol (5·45 g.), similarly prepared from the (−)-hydrogen phthalate (12·8 g.), had b. p. 113—115°/3 mm., n_D^{25} 1·5549. Rotatory powers are in Table 2.

(+)-1-*Ethyl*-3-*phenylprop*-2-*enyl Acetate*.—This was prepared from the (+)-alcohol, acetic anhydride, and pyridine at 100°, and had b. p. 158—159°/22 mm., n_D^{25} 1·5218, d_4^{25} 0·9720, d_4^{20} 0·9742, $[\alpha]_{5893}^{20}$ +120·1°, $[\alpha]_{5461}^{20}$ +146·8°, $[\alpha]_{4800}^{20}$ +211° (homogeneous; l, 0·5).

The corresponding (±)-*acetate* had b. p. 156—156·5°/21 mm., n_D^{25} 1·5249 (Found: C, 76·6; H, 7·8. $C_{12}H_{16}O_2$ requires C, 76·5; H, 7·9%).

(±)-1 : 2-*Dibromo*-1-*phenylpentan*-3-*ols*.—(*a*) A solution of bromine (40 g.) in chloroform (30 c.c.) was added to a stirred solution of the (±)-alcohol (40·5 g.) in chloroform (50 c.c.) maintained at 15°. Evaporation of the solvent and several crystallisations of the residue from light petroleum yielded the first *dibromo-alcohol*, fine needles (25·6 g.), m. p. 114—115° (Found: Br, 49·6. $C_{11}H_{14}OBr_2$ requires Br, 49·6%).

The original mother-liquor deposited both fine needles and hexagonal prisms, the latter being rather more soluble in light petroleum. Fractional crystallisation yielded the second *dibromo-alcohol*, hexagonal plates (39·9 g.), m. p. 93—94° (Found: Br, 49·85%).

(*b*) Pyridine bromide perbromide (9·35 g.) was added in portions to a solution of the (±)-alcohol (5 g.) in acetic acid (25 c.c.), and the mixture poured into ice–water and extracted with ether. By fractional crystallisation of the reaction product the two forms of the dibromo-alcohol were isolated with m. p. 92—93° and m. p. 114—115°, respectively: these values were unchanged when the compounds were mixed with the corresponding products obtained as in (*a*).

(*c*) *N*-Bromoacetamide (2 mols.) was added to a solution of the (±)-alcohol (2·5 g.) in chloroform (15 c.c.) under the light from a mercury arc. After several hours' illumination the solution was washed, dried, and evaporated: in this case also both forms of the (±)-dibromo-alcohol were obtained but in very poor yield.

By similar procedure the (+)-alcohol (8·0 g.) yielded (+)-1 : 2-dibromo-1-phenylpentan-3-ol as needles, m. p. 114—115° (5·8 g.), and (−)-1 : 2-dibromo-1-phenylpentan-3-ol as plates, m. p. 93—94° (9·15 g.), and the (−)-alcohol (5·0 g.) yielded (−)-1 : 2-dibromo-1-phenylpentan-3-ol as needles, m. p. 114—115° (2·80 g.), and (+)-1 : 2-dibromo-1-phenylpentan-3-ol as hexagonal plates, m. p. 93—94° (4·31 g.). Rotatory powers are in Table 3. (±)-2 : 3-Dibromo-1-ethyl-3-phenylpropyl acetate, obtained by addition of pyridine hydrobromide perbromide (1·9 g.) to a solution of the (±)-acetate (1·4 g.) in acetic acid (20 c.c.), was separated by fractional crystallisation from light petroleum into its two isomers, which formed fine rods, m. p. 164—165°, and short needles, m. p. 127—128° (see below).

TABLE 6. *Oxidation of the isomeric* 1 : 2-*dibromo*-1-*phenylpentan*-3-*ols to the isomeric pentan*-3-*ones.*

(i) (±)-Alcohol, m. p. 93—94°. Chromic anhydride (0·26 g.) was added in portions to a solution of the alcohol (0·5 g.) in acetic acid (2 c.c.) at 60°. Dilution with water followed by recrystallisation from ethanol yielded the ketone as needles (0·44 g.), m. p. 109—110°.
(ii) (±)-Alcohol, m. p. 114—115°, treated similarly, yielded the same ketone, m. p. 109—110°.
(iii) (+)-Alcohol, m. p. 114—115°, gave the (+)-ketone, m. p. 109—110°.
(iv) (−)-Alcohol, m. p. 93—94°, gave the (−)-ketone, m. p. 109—110°.
(v) (+)-Alcohol, m. p. 93—94°, gave the (+)-ketone, m. p. 109—110°.
(vi) (−)-Alcohol, m. p. 114—115°, gave the (−)-ketone, m. p. 109—110°.
Yields were about 90% in each case.
Determinations of mixed m. p.s were made where appropriate (Found: C, 41·3; H, 3·8; Br, 49·7. Calc. for $C_{11}H_{14}OBr_2$: C, 41·3; H, 3·7; Br, 49·9%).

(±)-1-*Phenylpent*-2-*en*-1-*ol*.—Prepared by the dropwise addition of a solution of pent-2-en-1-al (27 g.; b. p. 123—124°) in ether (100 c.c.) to a Grignard reagent [obtained from magnesium (8·76 g.) and bromobenzene (57·5 g.)] and maintained at 5—10°, the (±)-*alcohol* (37 g.) had b. p. 93—94°/0·7 mm., $n_D^{25°}$ 1·5270 (Found: C, 81·2; H, 8·6. $C_{11}H_{14}O$ requires C, 81·4; H, 8·6%). Its *p*-diphenylylurethane separated from ether–light petroleum in fine needles, m. p. 115—116° (Found: N, 3·7. $C_{24}H_{23}O_2N$ requires N, 3·9%). On admixture with the *p*-diphenylylurethane m. p. 150—151°, of the isomeric 1-phenylpent-1-en-3-ol it melted at 102—126°.

(±)-1-*Phenylpent*-2-*en*-1-*yl Hydrogen Phthalate*.—The (±)-alcohol (10 g.) was added to a solution of phthalic anhydride (9·2 g.) in warm pyridine (16 g.), and the mixture maintained at 40° during 2 hr. with occasional shaking in order to obtain a homogeneous solution as soon as possible. (These conditions are critical if isomeric change is to be avoided; at 95° isomeric

change is complete.) After being worked up as previously described, the *hydrogen phthalate* (18·9 g.) separated from ether–light petroleum in prismatic needles, m. p. 112—113° (when freshly prepared) (Found: C, 73·1; H, 5·9. $C_{19}H_{18}O_4$ requires C, 73·2; H, 5·8%). A mixture with the isomeric 1-ethyl-3-phenylprop-2-enyl hydrogen phthalate, of m. p. 109—110°, melted at 85—108°.

(−)-1-*Phenylpent*-2-*en*-1-*yl Hydrogen Phthalate*.—Quinidine (19·8 g.) was dissolved in a warm solution of the (±)-hydrogen phthalate (19 g.) in acetone (100 c.c.). The *quinidine salt* (20·5 g.) of the (−)-ester rapidly separated, and on recrystallisation from acetone (1500 c.c.) yielded the optically pure compound (17 g.) in cotton-wool-like needles, m. p. 150—151° (decomp.), $[\alpha]_{5893}$ +127°, $[\alpha]_{5461}$ +150·5°, $[\alpha]_{4358}$ +278° (*c*, 2·190 in $CHCl_3$; *l*, 2). A suspension of this salt (8·5 g.) in acetone (350 c.c.) was decomposed with ice-cold hydrochloric acid and yielded the (−)-hydrogen phthalate as an uncrystallisable oil, $[\alpha]_{5893}$ −4·35°, $[\alpha]_{5461}$ −6·45°, $[\alpha]_{4358}$ −13·6° (*c*, 5·50 in Et_2O; *l*, 2).

(−)-1-*Phenylpent*-2-*en*-1-*ol*.—The freshly prepared (−)-hydrogen phthalate (4·5 g.) was added to a solution of sodium ethoxide [from sodium (1·4 g.) in absolute ethanol (65 c.c.)] and heated on the steam-bath for 5 min. The liberated alcohol (1·9 g.), removed in a current of steam, had b. p. 94°/0·7 mm., n_D^{25} 1·5299, d_4^{25} 0·9894. Rotatory powers are in Table 2.

Its p-*diphenylylurethane* formed needles (from ether–light petroleum), m. p. 124—125°, $[\alpha]_D^{15}$ +14·1° (*c*, 1·277 in $CHCl_3$; *l*, 2). From the more soluble fractions of the quinidine salt there was obtained optically impure (+)-1-phenylpent-2-en-1-ol, b. p. 94—95°/0·7 mm., n_D^{25} 1·5290, $[\alpha]_D^{20}$ +3·64° (*l*, 0·5).

(±)-1-*Phenylpent*-2-*enyl Acetate*.—Prepared by interaction of the (±)-alcohol, pyridine, and *purified* acetic anhydride at 35° during 1½ hr., the (±)-acetate had b. p. 93—95°/1 mm., n_D^{25} 1·5069 (Found: C, 79·8; H, 7·9. Calc. for $C_{13}H_{16}O_2$: C, 76·5; H, 7·8%). When this acetate (2 g.) was heated with glacial acetic acid (3 g.) on the steam-bath for 4 hr. it was completely converted into the isomeric 1-ethyl-3-phenylprop-2-enyl acetate (confirmed by hydrolysis and formation of *p*-diphenylylurethane, m. p. and mixed m. p. 150—151°).

Rearrangement of 1-*Phenylpent*-2-*en*-1-*yl Hydrogen Phthalate to* 1-*Ethyl*-3-*phenylprop*-2-*enyl Hydrogen Phthalate*.—(i) A solution of the (±)-hydrogen phthalate (0·5 g.) in pyridine (0·5 c.c.) was heated on the steam-bath for 1·5 hr., cooled, and decomposed with hydrochloric acid. The product separated from carbon disulphide–light petroleum in glassy rhombs (0·25 g.), m. p. 109—110° alone or when mixed with authentic (±)-1-ethyl-3-phenylprop-2-enyl hydrogen phthalate.

(ii) A similar result was obtained when the (±)-hydrogen phthalate was kept in an evacuated desiccator at room temperature: the crystals become coated with a viscous oil within 30 min. and eventually turned pasty. Within 10 days the mass had re-solidified (m. p. 108—110°) and then separated from carbon disulphide–light petroleum in rhombs, m. p. 111—112°.

(iii) Optically pure (—)-hydrogen phthalate (0·5 g.) after 72 hr. at room temperature was hydrolysed by being heated with a solution of sodium ethoxide [from sodium (0·3 g.) and absolute ethanol (20 c.c.)], and the resultant alcohols (0·27 g.) were converted into their *p*-diphenylylurethanes. These, by fractional crystallisation from methylene chloride–light petroleum, were separated into the *p*-diphenylylurethanes of (−)-1-phenylpent-2-en-1-ol (0·14 g.), $[\alpha]_D$ +11·8° (*c*, 0·59 in $CHCl_3$; *l*, 2), and of a mixture of (±)- and (+)-1-phenylpent-1-en-3-ols having $[\alpha]_D$ +59·4° (*c*, 0·454 in $CHCl_3$; *l*, 2). This mixture was separated by crystallisation from benzene into its (+)-component (0·068 g.), m. p. 162—164°, $[\alpha]_D$ +144° (*c*, 0·67 in $CHCl_3$; *l*, 2) and the (±)-component (0·097 g.), m. p. 115—116°. The extent of racemisation in the recovered 1-phenylpent-2-en-1-ol was thus 16·4% whilst the retention of optical activity in the isomeric (+)-1-phenylpent-1-en-3-ol was 41%.

(iv) A solution of optically pure (−)-hydrogen phthalate (1·1932 g.) in chloroform (20 c.c.) had, when freshly prepared, α_D +0·18°; after 10 min., α_D +0·25°; after 24 hr., α_D +0·40° (unchanged after 3 days). During this period the chloroform solution deposited phthalic acid (0·11 g.); the recovered hydrogen phthalate {0·71 g.; $[\alpha]_D$ +7·6° (*c*, 1·365 in CS_2; *l*, 2)} was separated by crystallisation from carbon disulphide–light petroleum into optically pure (+)-1-ethyl-3-phenylprop-2-enyl hydrogen phthalate, m. p. 83°, $[\alpha]_D$ +53·3° (*c*, 1·400 in CS_2; *l*, 2), and the corresponding (±)-compound, m. p. 109—110°. The retention of optical activity is thus 14·2% (a duplicate experiment gave 13·8%).

(v) Duplication in benzene solution of experiment (iv) resulted in a retention of optical activity of 23·0%.

(vi) A specimen of the (−)-hydrogen phthalate (0·9 g.) after 15 days at room temperature was completely converted into the isomeric 1-ethyl-3-phenylprop-2-enyl hydrogen phthalate,

$[\alpha]_D$ +20·66° (*c*, 1·548; *l*, 1), which fractional crystallisation separated into the (±)- and the optically pure (+)-isomeride. The retention of optical activity in this reaction is 38·7%.

In another experiment the reaction was stopped before isomeric change was complete: the recovered 1-phenylpent-2-en-1-yl hydrogen phthalate had racemised to the extent of 16·4%.

Conversion of (+)-1-*Phenylpent*-2-*en*-1-*yl Hydrogen Phthalate.*—(a) *Into* (±)-1-*ethyl*-3-*phenylprop*-2-*enyl acetate.* A solution of the (+)-hydrogen phthalate (1·722 g.) in glacial acetic acid (20 c.c.) showed α_D +0·48° (*l*, 2) when freshly prepared and α_D +0·75° next day. This solution yielded phthalic acid (0·81 g.) and 1-ethyl-3-phenylprop-2-enyl acetate, b. p. 90—92°/0·9 mm., $\alpha_D^{20°}$ −0·15° (*l*, 0·5). The retention of optical activity is 0·25%.

(b) *Into* (−)-1-*ethyl*-3-*phenylprop*-2-*enyl methyl ether.* A solution of the (+)-hydrogen phthalate (1·70 g.; freshly prepared) in anhydrous methanol (20 c.c.) showed α_D^{20} +0·68° (*l*, 2), a value which gradually decreased:

hr.	0·5	1	1·5	2	3	4	22	30	170
α_D	+0·62°	0·57°	0·50°	0·45°	0·39°	0·33°	0·15°	0·12°	0·06°

After removal of the solvent, 1-*ethyl*-3-*phenylprop*-2-*enyl methyl ether*, b. p. 120°/22 mm., α_D^{20} −0·25° (*l*, 0·5), was recovered (Found: C, 81·7; H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%).

Rearrangement of (−)-1-*Phenylpent*-2-*en*-1-*ol to* (+)-1-*Phenylpent*-1-*en*-3-*ol in Acid Solution.*—To a solution of the (−)-alcohol (0·6482 g.) in dioxan (12 c.c.) was added hydrochloric acid (0·36 c.c.; constant b. p.) followed by distilled water to 20 c.c. The observed rotatory power oft he freshly prepared solution, α_D −0·54° (*l*, 2), changed steadily to +0·14° during 16 hr. and to +0·20° after 3 days. The recovered (+)-1-phenylpent-1-en-3-ol had n_D^{25} 1·5137, $\alpha_D^{14°}$ +2·05° (*l*, 0·5); the retention of optical activity thus being 59% (see next paragraph).

Racemisation of (+)-1-*Phenylpent*-1-*en*-3-*ol in Acid Solution.*—To a solution of the (+)-alcohol [0·9875 g.; $\alpha_D^{21°}$ +3·36° (*l*, 0·5)] in dioxan (12 c.c.) was added hydrochloric acid (0·36 c.c.) followed by distilled water to 20 c.c. The observed rotatory power, α_D −2·00° (*l*, 2), changed steadily to −0·75° after 65 hr., to −0·30° after 94 hr., to ±0° after 144 hr., to +0·16° after 234 hr., and to +0·23° after 20 days. The recovered alcohol had n_D^{25} 1·5182, $\alpha_D^{15°}$ +0·72° (*l*, 0·5), the loss in rotatory power being 79%. It thus follows that the isomeric (+)-1-phenylpent-1-en-3-ol produced in the preceding experiment would undergo partial racemisation after rearrangement. This implies that the rearrangement occurs with retention of optical activity considerably greater than 59%.

Conversion of (+)-1-*Phenyl*-*pent*-2-*en*-1-*ol.*—(a) *Into* (−)-1-*ethyl*-3-*phenylprop*-2-*enyl acetate.* A solution of the (+)-alcohol (*c*, 4·621; *l*, 2) in pure acetic acid had, when freshly prepared, α_D +0·49°: this fell after 6 hr. to +0·15° and after 60 hr. to −0·27° (constant). The recovered 1-ethyl-3-phenylprop-2-enyl acetate had b. p. 90—91°/0·7 mm., n_D^{25} 1·5221, α_D^{20} −1·30° (*l*, 0·5). The retention of optical activity is 3·7%.

(b) *Into* (−)-1-*ethyl*-3-*phenylprop*-2-*enyl* p-*diphenylylurethane.* A mixture of the (+)-alcohol (0·4 g.) and *p*-diphenylyl *iso*cyanate (0·5 g.) was heated on the steam-bath for 1 hr. The product, after crystallisation from benzene, had m. p. 147—160°, $[\alpha]_D$ −13·2° (*c*, 1·513 in $CHCl_3$; *l*, 2). By fractional crystallisation from benzene it was separated into the *p*-diphenylylurethanes of (i) (±)-1-phenylpent-1-en-3-ol, m. p. 152°, and (ii) (−)-1-phenylpent-1-en-3-ol, m. p. 163°, $[\alpha]_D$ −145° (*c*, 0·67 in $CHCl_3$; *l*, 2).

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The Synthesis of Alkylphenanthrenes Relevant to the Investigations on Methyl Vinhaticoate.

By F. E. KING and T. J. KING.

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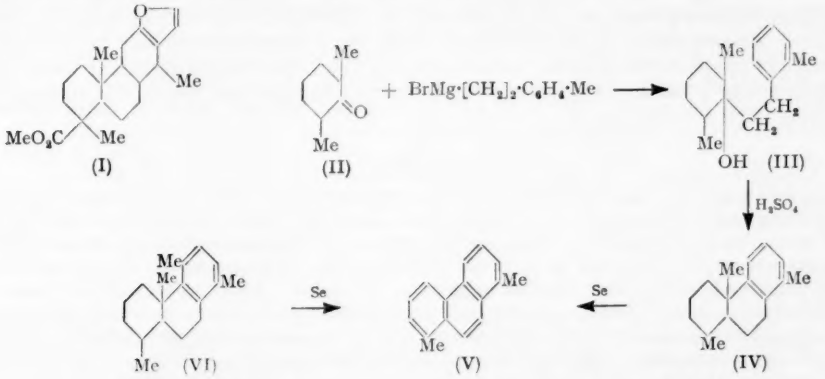
Syntheses have been effected by the Bogert–Cook method of 1 : 8-dimethyl-, 1-ethyl-8-methyl-, and 1 : 3 : 8-, 1 : 4 : 8-, and 2 : 4 : 8-trimethylphenanthrene. The appropriate phenylethylmagnesium bromides were condensed with 2 : 6-dimethyl*cyclo*hexanone and the products cyclised with sulphuric acid to octahydrophenanthrenes with an angular methyl group. These were aromatised with selenium except in the case of the 1 : 4 : 8 : 13-tetramethyl compound which gave 1 : 8-dimethylphenanthrene and required sulphur dehydrogenation for the isolation of the 1 : 4 : 8-trimethyl derivative.

A description is also included of the synthesis of 2-ethyl-1 : 5-dimethylnaphthalene.

THE structure assigned to methyl vinhaticoate (I) (King and King, *J.*, 1953, 4158) rests on information obtained by the aromatisation of various derivatives of the diterpene to alkylphenanthrenes, including 1 : 8-dimethyl- (Haworth, Mavin, and Sheldrick, *J.*, 1943, 454), 1-ethyl-8-methyl-, and 1 : 3 : 8-trimethyl-phenanthrene. The orientations of these end products of (I) were ascertained, as already described (King and King, *loc. cit.*), by comparison with authentic specimens which together with two other relevant compounds, namely, 1 : 4 : 8- and 2 : 4 : 8-trimethylphenanthrene, were synthesised for this purpose by the Bogert–Cook procedure. The following is an account of the synthetical operations.

The conditions employed are substantially those described by Papa, Perlman, and Bogert (*J. Amer. Chem. Soc.*, 1938, **60**, 319) and by Huebner and Jacobs (*J. Biol. Chem.*, 1947, **170**, 203), and the reaction sequence (II)—(V) relating to the preparation of 1 : 8-dimethylphenanthrene illustrates the general method.



The choice of 2 : 6-dimethyl*cyclo*hexanone (II) rather than of the isomeric 2 : 2-dimethyl compound as a component of the synthesis depends on its considerably superior reactivity in the Grignard reaction. An improved preparation of the required ketone (II) from 2-methyl*cyclo*hexanone was based on the method of Sen and Mondal (*J. Indian Chem. Soc.*, 1928, **5**, 609; see also Cornforth and Robinson, *J.*, 1949, 1859). Formylation and *C*-methylation at the 6-position followed by removal of the formyl group gave 2 : 6-dimethyl-*cyclo*hexanone (over-all yield 45%), unchanged 2-methyl*cyclo*hexanone being removed by extraction as the bisulphite compound. The 2-arylethyl bromides were obtained by a standard procedure from the appropriately substituted arylmagnesium bromides and ethylene oxide, phosphorus tribromide being used to esterify the resulting arylethyl alcohols. Ring-closure of the alcohols, *e.g.*, (III), was carried out with 85% sulphuric acid, and the

octahydrophenanthrenes, for example, (IV), were aromatised with the loss of the angular substituent by heating them with selenium. The intermediate tertiary alcohols and the octahydrophenanthrenes were, with one exception, liquids consisting presumably of mixed stereoisomers; unsatisfactory analytical results were sometimes obtained owing to the presence of varying amounts of diarylbutanes formed by self-condensation of the halides in the Grignard reaction. All the phenanthrenes were crystalline solids characterised by picrates and trinitrobenzene and trinitrofluorenone derivatives. Where quantities allowed, the phenanthraquinones and derived quinoxalines were also prepared.

No difficulties were encountered in the synthesis of 1 : 8-dimethyl-, 1-ethyl-8-methyl-, and 1 : 3 : 8-trimethyl-phenanthrene, but selenium dehydrogenation of the tetramethyl derivative (VI) yielded primarily the 1 : 8-dimethyl compound (V) and although some of the expected 1 : 4 : 8-trimethylphenanthrene was undoubtedly present its isolation was impracticable. Even after most careful purification of the initial bromo-*p*-xylene, which from the production of (V) was at first supposed to contain *o*-bromotoluene, the formation of 1 : 8-dimethylphenanthrene continued. However, with the substitution of sulphur as dehydrogenating agent 1 : 4 : 8-trimethylphenanthrene was readily obtained at 240°; loss of the 4-methyl group can therefore be attributed to the higher temperature (300°) required in the selenium reaction.

The expulsion of methyl from an already aromatised ring during dehydrogenation with selenium has not previously been reported, even in the closely comparable synthesis of 1 : 4-dimethylphenanthrene (Papa *et al.*, *loc. cit.*). In order to determine whether elimination of the 4-methyl group occurs in other trimethylphenanthrenes the preparation of the 2 : 4 : 8-trimethyl derivative was undertaken, but not only was the trimethylphenanthrene readily obtained from the selenium dehydrogenation of the requisite intermediate, but no trace of the alternative well-characterised dimethyl compound (pimanthrene) was detected in the reaction mixture.

The synthesis of 2-ethyl-1 : 5-dimethylnaphthalene was also included in this project since it was of interest as a potential dehydrogenation product of a dicarboxylic acid obtained in the oxidative degradation of methyl vinhaticoate. 2-Ethyl-5-methyl-1-tetralone (Harvey, Heilbron, and Wilkinson, *J.*, 1930, 423), prepared by a slight modification of the original method, was treated with methylmagnesium iodide. The resulting mixture of ethyldimethyltetralol and ethyl 3 : 4-dihydrodimethylnaphthalene when heated with selenium gave the liquid 2-ethyl-1 : 5-dimethylnaphthalene which was characterised by crystalline derivatives.

Experimental

2 : 6-*Dimethyl*cyclo*hexanone* (II).—2-Hydroxymethylene-6-methyl*cyclo*hexanone, prepared by the method of Johnson and Posvic (*J. Amer. Chem. Soc.*, 1947, **69**, 1361) and once distilled, was methylated with excess of methyl iodide–potassium carbonate in boiling acetone for 12 hr. The acetone was then distilled off, the residue treated with a large excess of 20% aqueous sodium hydroxide, and the solution distilled in steam. The distillate was extracted with ether, and the ethereal solution repeatedly shaken with saturated aqueous sodium hydrogen sulphite until no more ketone was extracted. The ethereal solution was then dried and distilled, pure 2 : 6-dimethyl*cyclo*hexanone (yield 45%) being collected between 172—173° (lit., b. p. 170—171°). The product formed a 2 : 4-dinitrophenylhydrazone, m. p. 149—150° (Birch, *J.*, 1947, 1642, gives m. p. 149—150°).

2 : 6-*Dimethyl*-1-(2-o-*tolylethyl*)cyclo*hexanol* (III).—An ethereal solution of 2 : 6-dimethyl-*cyclo*hexanone (10 g., 1 mol.) was added to one of Grignard reagent prepared from 2-*o*-tolylethyl bromide (16 g.) (cf. Shoesmith and Connor, *J.*, 1927, 1768), and the mixture set aside overnight. After 6 hr.' boiling, the solution was treated with ice and dilute hydrochloric acid, and the dried ethereal layer was distilled. The *alcohol* (III), b. p. 150—160° (bath)/1 mm., consisted of a pale yellow viscous oil (11 g., 58%) which became partly crystalline. The solid (3 g.) crystallised from a very small volume of methanol in colourless prisms, m. p. 55—57° (Found: C, 83·3; H, 10·3. $C_{17}H_{26}O$ requires C, 82·9; H, 10·6%). Redistillation of the oil from which the solid had separated gave a similar product (Found: C, 82·9; H, 10·0%) but which did not crystallise.

1 : 8 : 12-*Trimethyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene* (IV).—The crude alcohol (III) (10 g.) was slowly added to ice-cold sulphuric acid (85%; 30 c.c.) with constant shaking.

After 15 min. the mixture was extracted with light petroleum (b. p. 60—80°), and the petroleum solution thoroughly washed, first with 85% sulphuric acid, and then with water. The dried liquid was distilled, giving the *hydrophenanthrene* (IV) (7·7 g., 83%), b. p. after redistillation from sodium 204—206°/30 mm. (Found: C, 89·3; H, 10·1. $C_{17}H_{24}$ requires C, 89·4; H, 10·6%).

1 : 8-*Dimethylphenanthrene* (V).—The hydrophenanthrene (IV) (2 g.) was heated with selenium (4 g.) for 40 hr. at 320—340° (metal-bath). The product was extracted with chloroform and isolated by evaporation of the filtered solution (charcoal) as a light brown crystalline solid (1·1 g.) which by crystallisation from benzene or acetic acid gave 1 : 8-dimethylphenanthrene (V) (1 g., 55%) as colourless shining plates, m. p. 191—192° (Found: C, 92·9; H, 6·7. Calc. for $C_{16}H_{14}$: C, 93·2; H, 6·8%); it gave a picrate, m. p. 152° (lit., m. p. 151—152°), 1 : 8-dimethylphenanthraquinone, m. p. 189—190° (lit., m. p. 190°), and a quinoxaline derivative, m. p. 190—191° (sintering at 187°) (lit., m. p. 178°) (Found: C, 85·3; H, 4·9. Calc. for $C_{22}H_{16}N_2$: C, 85·7; H, 5·2%). The *trinitrobenzene* derivative, bright yellow needles from ethanol, had m. p. 173—174° (Found: C, 63·5; H, 3·7. $C_{16}H_{14},C_6H_3O_6N_3$ requires C, 63·0; H, 4·1%), and the *trinitrofluorenenone* derivative, stout orange needles from xylene–ethanol, had m. p. 193—194° (Found: C, 66·8; H, 3·9. $C_{16}H_{14},C_{13}H_5O_7N_3$ requires C, 66·8; H, 3·7%).

1-[2-(2 : 4-*Dimethylphenyl*)*ethyl*]-2 : 6-*dimethyl*cyclo*hexanol*.—2 : 6-Dimethyl*cyclo*hexanone (15 g., 1·2 mol.) and the Grignard reagent from 2-(2 : 4-dimethylphenyl)ethyl bromide (21·3 g.) (cf. Ruzicka, Ehmann, and Mörgeli, *Helv. Chim. Acta*, 1933, **16**, 314) gave, by the method previously described, the *alcohol* (13·0 g., 50%) as a colourless viscous oil, b. p. 156—157°/1 mm. (Found: C, 83·2; H, 10·6. $C_{18}H_{28}O$ requires C, 83·0; H, 10·8%).

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-1 : 6 : 8 : 12-*tetramethylphenanthrene*.—The above alcohol (12·4 g.), treated with sulphuric acid as previously described, gave the *hydrophenanthrene* (10 g., 86%) as a colourless oil, b. p. 130—140°/1 mm. After 3 days at room temperature, crystalline solid had separated, and the residue from this, when redistilled from sodium, had b. p. 130—135°/1 mm. (Found: C, 89·5; H, 10·7. $C_{18}H_{26}$ requires C, 89·2; H, 10·8%). The separated solid (0·5 g.) crystallised from ethanol in long rods, m. p. 70—71° (Found: C, 89·8; H, 10·0. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%), presumably consisting of 1 : 4-*di*-(2 : 4-*dimethylphenyl*)-*butane*.

1 : 3 : 8-*Trimethylphenanthrene*.—The foregoing hydrophenanthrene (2 g.) was heated with selenium (4 g.) at 320—340° for 24 hr., and the product extracted with ether and distilled. The fraction of b. p. 120—160° (bath)/0·2 mm. crystallised from methanol, giving 1 : 3 · 8-*trimethylphenanthrene* (0·9 g., 50%) as colourless needles, m. p. 116° (Found: C, 92·3; H, 7·2. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%); the *picrate*, orange needles from ethanol, had m. p. 174—175° (Found: C, 61·8; H, 4·2. $C_{17}H_{16},C_6H_3O_7N_3$ requires C, 61·5; H, 4·3%); the *trinitrobenzene* derivative, yellow needles from ethanol, had m. p. 188° (Found: C, 63·3; H, 4·3. $C_{17}H_{16},C_6H_3O_6N_3$ requires C, 63·7; H, 4·4%); and the *trinitrofluorenone* derivative, orange needles from xylene–ethanol, had m. p. 199° (Found: C, 67·6; H, 4·25. $C_{17}H_{16},C_{13}H_5O_7N_3$ requires C, 67·3; H, 4·0%). 1 : 3 : 8-*Trimethylphenanthraquinone* crystallised from ethanol or acetic acid in orange needles, m. p. 180° (Found: C, 81·3; H, 6·0. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%); the derived *quinoxaline*, pale yellow long needles from ethanol or acetic acid, had m. p. 146—147° (Found: C, 85·2; H, 5·2. $C_{23}H_{18}N_2$ requires C, 85·7; H, 5·6%).

2-o-*Ethylphenylethyl Bromide*.—2-*o*-Ethylphenylethyl alcohol (Kutz, Nickels, McGovern, and Corson, *J. Org. Chem.*, 1951, **16**, 699), b. p. 76—78°/0·1 mm. (lit., b. p. 127·5°/20 mm.) [*α-naphthylurethane*, colourless needles from light petroleum (b. p. 60—80°), m. p. 104° (Found: C, 78·6; H, 6·6. $C_{21}H_{21}O_2N$ requires C, 79·0; H, 6·6%)], was converted with phosphorus tribromide in the usual way into the *bromide* (65%), b. p. 68°/0·1 mm., n_D^{20} 1·5562 (Found: Br, 37·0. $C_{10}H_{13}Br$ requires Br, 37·5%).

1-(2-o-*Ethylphenylethyl*)-2 : 6-*dimethyl*cyclo*hexanol*.—2 : 6-Dimethyl*cyclo*hexanone (16 g., 1·2 mol.) and Grignard reagent from the above bromide (23 g.) gave the cyclo*hexanol* (14·4 g., 51%) as a colourless oil, b. p. 122—124°/0·05 mm. (Found: C, 83·3; H, 10·9. $C_{18}H_{28}O$ requires C, 83·0; H, 10·8%).

8-*Ethyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-1 : 12-*dimethylphenanthrene*.—The foregoing alcohol (13·8 g.) when treated with sulphuric acid in the usual way gave the *hydrophenanthrene* as a colourless oil (11·3 g., 88%), b. p. 106—110°/0·05 mm. (Found: C, 89·0; H, 10·6. $C_{18}H_{26}$ requires C, 89·2; H, 10·8%).

1-*Ethyl*-8-*methylphenanthrene*.—The above hydrophenanthrene (2 g.) was heated with selenium (4 g.) at 320—340° for 48 hr. Distillation of the product followed by crystallisation from methanol gave 1-*ethyl*-8-*methylphenanthrene* (1·0 g., 55%) as glistening plates, m. p. 106° (Found: C, 92·6; H, 7·5. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%); the *picrate*, orange needles from

ethanol, had m. p. 124—125° (Found: C, 61·0; H, 4·4. $C_{17}H_{16},C_6H_3O_7N_3$ requires C, 61·5; H, 4·3%); the *trinitrobenzene* derivative, yellow needles from ethanol, had m. p. 145—146° (Found: C, 63·6; H, 4·2. $C_{17}H_{16},C_6H_3O_6N_3$ requires C, 63·7; H, 4·4%); and the *trinitrofluorenone* derivative, orange needles from xylene–ethanol, had m. p. 158—159° (Found: C, 67·0; H, 3·8. $C_{17}H_{16},C_{13}H_5O_7N_3$ requires C, 67·3; H, 4·0%). 1-*Ethyl*-8-*methylphenanthraquinone*, orange plates from ethanol, had m. p. 154—155° (Found: C, 81·9; H, 5·9. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%); and the derived *quinoxaline*, pale yellow leaflets from acetic acid, or felted needles from ethanol, had m. p. 130° (Found: C, 85·8; H, 5·9. $C_{23}H_{18}N_2$ requires C, 85·7; H, 5·6%).

1-[2-(2 : 5-*Dimethylphenyl*)*ethyl*]-2 : 6-*dimethyl*cyclo*hexanol*.—2 : 6-Dimethyl*cyclo*hexanone (6 g., 1·7 mol.) and Grignard reagent from 2-(2 : 5-dimethylphenyl)ethyl bromide (9 g.) (Papa *et al.*, *loc. cit.*), made from rigorously purified bromo-*p*-xylene, gave the cyclo*hexanol* as a colourless oil (5·9 g., 54%), b. p. 158—161°/1 mm. (Found: C, 83·5; H, 10·1. $C_{18}H_{28}O$ requires C, 83·0; H, 10·8%).

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-1 : 5 : 8 : 12-*tetramethylphenanthrene*.—Ring closure of the above alcohol (5·5 g.) with sulphuric acid gave the *hydrophenanthrene* as a colourless oil (4·2 g., 82%), b. p. 130—135°/1 mm. (Found: C, 88·9; H, 10·3. $C_{18}H_{26}$ requires C, 89·2; H, 10·8%).

1 : 4 : 8-*Trimethylphenanthrene*.—The relevant hydrophenanthrene (2 g.) was heated with sulphur (1·05 g.) at 220—240° for 3 hr. The product was distilled and the yellow oily fraction, b. p. 110—150° (bath)/0·05 mm., converted into the orange *trinitrobenzene* derivative which after four crystallisation from ethanol had m. p. 160—161° (Found: C, 63·9; H, 4·6. $C_{17}H_{16},C_6H_3O_6N_3$ requires C, 63·7; H, 4·4%), and when pure was of the usual bright yellow colour. The trinitrobenzene derivative was decomposed by passage of its solution in benzene down an alumina column followed by elution with light petroleum (b. p. 60—80°), the eluate when evaporated giving 1 : 4 : 8-*trimethylphenanthrene* (0·35 g., 19%). After three crystallisations from methanol the pure hydrocarbon formed colourless needles, m. p. 64° (Found: C, 92·8; H, 7·5. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%); the *picrate*, orange needles from ethanol, had m. p. 136—137° (Found: C, 62·0; H, 4·5. $C_{17}H_{16},C_6H_3O_7N_3$ requires C, 61·5; H, 4·3%); and the *trinitrofluorenone* derivative, orange needles from ethanol, had m. p. 165—166° (Found: C, 67·0; H, 3·7. $C_{17}H_{16},C_{13}H_5O_7N_3$ requires C, 67·3; H, 4·0%).

When the dehydrogenation was carried out with selenium in the usual way the distillate deposited crystalline material (0·15 g.) which was identified as 1 : 8-dimethylphenanthrene. The mother-liquors from the crystallisation of the dimethyl compound were worked up through the trinitrobenzene derivative but, although a product of the correct m. p. was obtained, regeneration gave a hydrocarbon still appreciably contaminated with the dimethylphenanthrene, which, owing to its low solubility, could not be removed by crystallisation.

2-(3 : 5-*Dimethylphenyl*)*ethyl Bromide*.—2-(3 : 5-Dimethylphenyl)ethyl alcohol (cf. Matsui, *J. Soc. Chem. Ind. Japan*, 1942, **45**, 300), b. p. 130°/15 mm. (lit., b. p. 123—125°/9 mm.), with phosphorus tribromide in the usual way gave the *bromide* (50%), b. p. 75—78°/0·5 mm., n_D^{20} 1·5452 (Found: C, 56·4; H, 6·1. $C_{10}H_{13}Br$ requires C, 56·3; H, 6·1%).

1-[2-(3 : 5-*Dimethylphenyl*)*ethyl*]-2 : 6-*dimethyl*cyclo*hexanone*.—2 : 6-Dimethyl*cyclo*hexanone (10 g., 1·2 mol.) and Grignard reagent from the foregoing bromide (14·9 g.) gave the cyclo*hexanol* (4·8 g., 26%) as a colourless oil, b. p. 160—162°/1·5 mm. (Found: C, 83·4; H, 10·6. $C_{18}H_{28}O$ requires C, 83·0; H, 10·8%).

1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-1 : 5 : 7 : 12-*tetramethylphenanthrene*.—Treatment of the requisite alcohol (4·6 g.) with sulphuric acid gave the *hydrophenanthrene* as a colourless oil (3·1 g., 72%), b. p. 100—102°/0·04 mm. (Found: C, 89·1; H, 10·4. $C_{18}H_{26}$ requires C, 89·2; H, 10·8%).

2 : 4 : 8-*Trimethylphenanthrene*.—The octahydrotetramethylphenanthrene (2 g.) was dehydrogenated with selenium (4 g.) at 320—340° for 24 hr. The product distilled as an uncrystallisable oil which was converted into the *trinitrobenzene* derivative; after three crystallisations from ethanol this separated as yellow needles, m. p. 150—151° (Found: C, 63·6; H, 4·2. $C_{17}H_{16},C_6H_3O_6N_3$ requires C, 63·7; H, 4·4%). The hydrocarbon was regenerated from this derivative on an alumina column in the usual way, and the 2 : 4 : 8-*trimethylphenanthrene* (0·7 g., 39%) so obtained separated from methanol in large prisms, m. p. 50° (Found: C, 92·2; H, 7·6. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%); the *picrate*, orange needles from ethanol, had m. p. 135° (Found: C, 61·6; H, 4·2. $C_{17}H_{16},C_6H_3O_7N_3$ requires C, 61·5; H, 4·3%); and the *trinitrofluorenone* derivative, orange needles or slender red prisms from xylene–ethanol, had m. p. 178—179° (Found: C, 67·6; H, 4·0. $C_{17}H_{16},C_{13}H_5O_7N_3$ requires C, 67·3; H, 4·0%).

2-Ethyl-5-methyl-1-tetralone.—2-*o*-Tolylethyl bromide and the sodio-derivative of diethyl ethylmalonate, condensed in the usual way, gave diethyl α-ethyl-α-(2-*o*-tolylethyl)malonate (55%) as a colourless oil, b. p. 192—194°/11 mm., n_D^{17} 1·4917, which was converted by the usual methods into the corresponding monocarboxylic acid and thence into the tetralone (Harvey *et al., loc. cit.*); the 2 : 4-*dinitrophenylhydrazone*, bright orange prisms from ethanol, had m. p. 172—173° (Found: C, 61·8; H, 5·1. $C_{19}H_{20}O_4N_4$ requires C, 61·9; H, 5·5%).

2-Ethyl-1 : 5-dimethylnaphthalene.—2-Ethyl-5-methyl-1-tetralone (5 g.) was treated in boiling ether for 6 hr. with excess of methylmagnesium iodide. The product (3·8 g.) boiled from 140° to 152°/12 mm., presumably owing to partial dehydration (cf. Ruzicka and Ehmann, *Helv. Chim. Acta*, 1932, **15**, 140), and without further treatment was dehydrogenated with selenium (3 g.) at 300—320° for 24 hr. The *naphthalene* (1·5 g., 30%) isolated by distillation, b. p. 135—137°/12 mm., n_D^{20} 1·6023 (Found: C, 91·9; H, 8·7. $C_{14}H_{16}$ requires C, 91·3; H, 8·7%), was purified by regeneration from the *trinitrobenzene* derivative, yellow leaflets (from ethanol), m. p. 112—113° (Found: C, 60·7; H, 4·5. $C_{14}H_{16}.C_6H_3O_6N_3$ requires C, 60·5; H, 4·8%), but it failed to crystallise. The very soluble *picrate* crystallised in orange needles as the alcoholate from a small volume of ethanol (removal of the solvent entailing decomposition), and had m. p. 82—84° (Found: C, 57·1; H, 5·2. $C_{14}H_{16}.C_6H_3O_7N_3.C_2H_6O$ requires C, 57·5; H, 5·5%). The *trinitrofluorenone* derivative, prepared in ethanol, separated as orange needles, m. p. 104—105°, decomposed by recrystallisation (Found: C, 64·7; H, 4·2. $C_{14}H_{16}.C_{13}H_5O_7N_3$ requires C, 64·9; H, 4·2%).

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THE UNIVERSITY, NOTTINGHAM. [*Received, December 28th*, 1953.]

Acrylonitrile in Organic Syntheses. Part I. Synthesis of 3a : 4 : 5 : 6-*Tetrahydroperinaphthane*-3a-*carboxylic Acid.*

By A. D. CAMPBELL.

[Reprint Order No. 5041.]

Acid hydrolysis of γ-cyano-γ-phenylpimelonitrile (III) gave α-2-carboxyethyl-α-phenylglutarimide (IV) which was cyclised to 1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene-1-*spiro*-α-glutarimide (V). γ-Carboxy-γ-phenylpimelic acid (VI), obtained by prolonged hydrolysis of (III) or (IV) by acid or alkali, was cyclised to 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII). After reduction by the Clemmensen procedure (VII) was further cyclised to 3*a* : 4 : 5 : 6-tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid (X). This keto-acid (X) gave 3*a* : 4 : 5 : 6-tetrahydroperinaphthane-3*a*-carboxylic acid on reduction. A method for the synthesis of α-phenylglutaric anhydride is described.

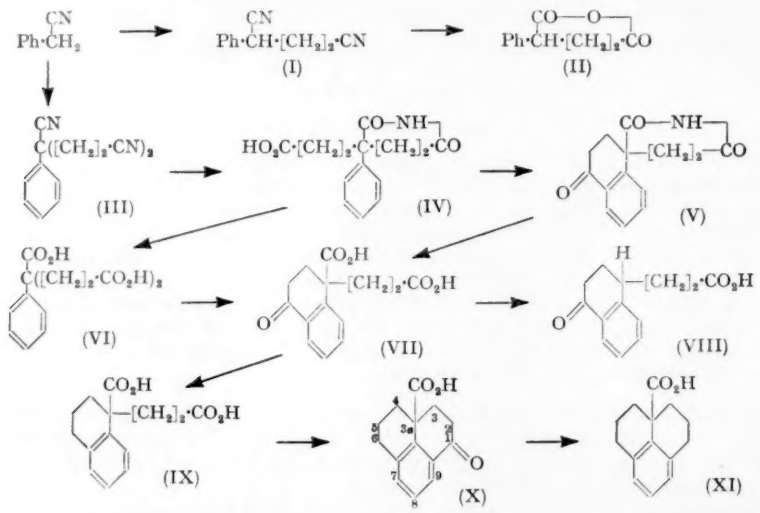
ACRYLONITRILE is a reagent whose many reactions (Bruson, *Organic Reactions*, 1949, **5**, 77) have found numerous uses in synthetic organic chemistry. The present communication describes the use of acrylonitrile in the preparation of a number of derivatives of tetrahydronaphthalene and tetrahydroperinaphthane.

When equimolar quantities of acrylonitrile and phenylacetonitrile reacted in *tert.*-butyl alcohol containing an alkaline catalyst (methyl-alcoholic potassium hydroxide or Triton B) at temperatures from 15° to 100° the product was invariably γ-cyano-γ-phenylpimelonitrile (III). By using Roger's method (*Chem. Abs.*, 1949, **43**, 3446; U.S.P. 2,460,536/1949) in which acrylonitrile is added to an excess of boiling phenylacetonitrile in the presence of sodium cyanide a 65% yield of α-phenylglutaronitrile (I) has been obtained. Where dicyanoethylation is possible it is normally difficult to isolate the monocyanoethylation product (Bruson, *op. cit.*) but it appears that elevated temperatures favour monosubstitution. However, Koelsch (*J. Amer. Chem. Soc.*, 1943, **65**, 437) obtained a 20—33% yield of α-phenylglutaronitrile by treating acrylonitrile with phenylacetonitrile in molar proportions in the absence of a solvent (sodium ethoxide as catalyst), and when ether was used as solvent the yield rose to 36%. The effect of temperature

on the course of the cyanoethylation reaction is being further investigated. Hydrolysis of the nitrile (I) by aqueous sulphuric acid gave α-phenylglutaric acid which was isolated as the anhydride (II): Hornig and Finelli (*ibid.*, 1949, **71**, 3204) prepared this anhydride by a similar but more indirect method, converting the phenylacetonitrile into ethyl α-cyano-α-phenylacetate where only monocyanoethylation is possible.

γ-Cyano-γ-phenylpimelonitrile (III), the condensation product formed when two mols. of acrylonitrile condense with one of phenylacetonitrile (Bruson, *ibid.*, 1942, **64**, 2858), resisted normal hydrolysis. Prolonged hydrolysis by alkali gave γ-carboxy-γ-phenylpimelic acid, but acid hydrolysis gave, after 6 hr.' refluxing, α-2-carboxyethyl-α-phenylglutarimide (IV) which could be converted into the required acid by further prolonged hydrolysis with acid or alkali. This imide was monobasic to phenolphthalein and the keto-imide, 1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene-1-*spiro*-α-glutarimide (V), formed on cyclisation with sulphuric acid was neutral to phenolphthalein although it dissolved in alkali. The keto-imide (V) was readily hydrolysed to 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII) by aqueous alkali.

Cyclisation of γ-carboxy-γ-phenylpimelic acid (VI), previously prepared by the oxidation of γ-acetyl-γ-phenylpimelic acid (Bruson, *loc. cit.*), with anhydrous hydrogen fluoride or concentrated sulphuric acid at 70° gave a good yield of 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII), which exists in two crystalline forms; no perinaphthane derivative was isolated. It is interesting that although Manske (*ibid.*, 1931, **53**, 1104) obtained mainly 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene and only a very small yield of 3*a* : 4 : 5 : 6-tetrahydro-1 : 6-dioxoperinaphthane von Braun and Weissbach (*Ber.*, 1931, **64**, 1785) claimed that this cyclisation produced mainly the



diketone. In general, *meta*-directing groups inhibit intermolecular acylation (Johnson, *Organic Reactions*, 1944, **2**, 120). Cyclisation of γ-carboxy-γ-phenylpimelic acid with concentrated sulphuric acid at 100° gave a low yield of the expected keto-acid together with a compound which was an acid–base indicator. Analytical figures suggest that it is the potassium salt of a sulphonic acid and may be an oxidation product of the doubly cyclised 3*a* : 4 : 5 : 6-tetrahydro-1 : 6-dioxoperinaphthane-3*a*-carboxylic acid.

1-2'-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid was readily decarboxylated to 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene (VIII), previously prepared by Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1109) as one of the products from the cyclisation of γ-phenylpimelic acid. Although the carboxyl group attached to the

quaternary carbon atom was easily eliminated in this case, attempts to decarboxylate γ-carboxy-γ-phenylpimelic acid with copper powder in quinoline at 210° were unsuccessful.

By using the Clemmensen–Martin procedure (*ibid.*, 1936, **58**, 1438) 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII) was reduced to the acid (IX) and then cyclised with anhydrous hydrogen fluoride to 3*a* : 4 : 5 : 6-tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid (X), which was very easily decarboxylated by heat. The 2 : 4-dinitrophenylhydrazone of this keto-acid was decarboxylated in boiling ethanol, giving the 2 : 4-dinitrophenylhydrazone of 3*a* : 4 : 5 : 6-tetrahydroperinaphthan-1-one; this ketone had been prepared by von Braun and Reutter (*Ber.*, 1926, **59**, 1922) by cyclisation of 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydronaphthalene. 3*a* : 4 : 5 : 6-Tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid was reduced by the Clemmensen procedure to 3*a* : 4 : 5 : 6-tetrahydroperinaphthane-3*a*-carboxylic acid (XI) in which the carboxyl group is attached to a quaternary carbon atom at the point of fusion of the two saturated rings.

Experimental

α-Phenylglutaric Anhydride (II).—A mixture of phenylacetonitrile (150 g.) and sodium cyanide (1 g.) was heated (oil-bath) to 225°; water (0·5 c.c.) and then acrylonitrile (14 g.) were added dropwise with stirring. The mixture was stirred at 225° for 30 min. and then fractioned under reduced pressure, to give α-phenylglutaronitrile (30 g.), b. p. 200—205°/15 mm., as a colourless liquid. Rogers (*loc. cit.*) gives b. p. 163°/1 mm. The nitrile (28 g.) was refluxed with water (40 c.c.), concentrated sulphuric acid (40 c.c.), and glacial acetic acid (40 c.c.) for 5 hr., poured into water, extracted with ether–ethyl acetate, and dried and the solvent was removed under reduced pressure. The residue was refluxed with acetic anhydride (30 c.c.) for ½ hr. and distilled. The anhydride, b. p. 235—240°/15 mm. (26 g.), had m. p. 95°. Hornig and Finelli (*loc. cit.*) give m. p. 95—96°.

γ-Carboxy-γ-phenylpimelic Acid (VI).—(*a*) γ-Cyano-γ-phenylpimelonitrile (12 g.) was refluxed for 60 hr. with potassium hydroxide (20 g.) in water (100 c.c.). The mixture of acid and potassium chloride which separated on acidification with concentrated hydrochloric acid was filtered off and the acid was taken up in acetone. Evaporation gave an oil which crystallised from nitromethane, to give the acid (8 g.), m. p. 154° (Bruson, *loc. cit.*, gives m. p. 154°). (*b*) γ-Cyano-γ-phenylpimelonitrile (10 g.) was refluxed for 40 hr. with concentrated sulphuric acid (50 g.), glacial acetic acid (50 g.), and water (50 c.c.). The mixture was cooled and poured on cracked ice, and the solid which separated was filtered off and recrystallised from water, to give the acid (7·5 g.), m. p. 153—154°.

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxo*-1-*naphthoic acid* (VII).—(*a*) γ-Carboxy-γ-phenylpimelic acid (10 g.) was treated with anhydrous hydrogen fluoride (approx. 100 g.) in a copper beaker. After 48 hr. the remaining hydrogen fluoride was allowed to evaporate, ice was added, and the product extracted with ether. The solid obtained on evaporation of the ether was recrystallised from water, to give the *keto-acid* (6 g.), m. p. 135—136°. Further recrystallisation from water or ethyl acetate gave white cubes or needles, respectively, both of m. p. 167° (Found: equiv., 125; C, 64·2; H, 5·5%. $C_{14}H_{14}O_5$ requires equiv., 131; C, 64·1; H, 5·3%). The acid of m. p. 135—136° gave a similar equivalent weight. Both acids gave a *semicarbazone*, m. p. 239—240° (decomp.), as fine white crystals from ethanol (Found: N, 13·0. $C_{15}H_{17}O_5N_3$ requires N, 13·2%), and a 2 : 4-*dinitrophenylhydrazone* as orange-red crystals, m. p. 208° with resolidification, remelting at 225—226° (Found: N, 12·8. $C_{20}H_{18}O_8N_4$ requires N, 12·7.

(*b*) γ-Carboxy-γ-phenylpimelic acid (10 g.) was warmed to 70—80° for 2 hr. with concentrated sulphuric acid (50 c.c.). The mixture was poured on cracked ice, and the acid which separated was filtered off and recrystallised from water; it melted at 135—136°, resolidifying immediately to remelt at 166—167°.

(*c*) When the above reaction was carried out at 100° the deep red solution formed when the product was poured on ice water was extracted with ether–ethyl acetate. Extraction of the organic layer with concentrated aqueous potassium hydroxide, followed by acidification, gave the keto-acid (VII) together with a red powder which was sparingly soluble in ethyl acetate. Recrystallisation of this red compound from water gave a brick-red hygroscopic powder, decomp. >300° (Found: C, 50·2; H, 3·2; K, 12·2%). This compound which also contained sulphur acts as an acid–base indicator changing colour at pH 4·5—5 from a pink fluorescence in alkali

to a yellow fluorescence in acid. A very marked colour change is noticed in acid–base titrations containing 0·1 mg. of the compound per 100 c.c. of solution.

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthoic Acid* (IX).—1-2′-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (6 g.) was refluxed for 6 hr. with amalgamated zinc (20 g.), concentrated hydrochloric acid (35 c.c.), water (15 c.c.), acetic acid (2 c.c.), and toluene (10 c.c.). The acid remaining after evaporation of the combined toluene layer and ether-extracts of the aqueous layer failed to crystallise. It was taken up in aqueous alkali (charcoal), reprecipitated, and taken up in ether. A semisolid *acid* remained after evaporation of the ether (Found: C, 67·5; H, 6·6. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%).

3a : 4 : 5 : 6-*Tetrahydro*-1-*oxoperinaphthane*-3a-*carboxylic Acid* (X).—The preceding acid (4 g.) was treated with anhydrous hydrogen fluoride (approx. 60 g.) in a copper beaker for 20 hr. The remaining hydrogen fluoride was allowed to evaporate, ice was added, and the product was extracted with ether and taken up in aqueous sodium hydroxide (charcoal), and reprecipitated by acid. Clusters of white needles of the *keto-acid* (2·5 g.), m. p. 203°, separated on cooling (Found: equiv., 223; C, 73·1; H, 6·4%. $C_{14}H_{14}O_3$ requires equiv., 230; C, 73·1; H, 6·1%). It gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 266° (with previous darkening), as red needles from warm ethanol (Found: N, 13·9. $C_{20}H_{18}O_6N_4$ requires N, 13·7%).

3a : 4 : 5 : 6-*Tetrahydroperinaphthan*-1-*one*.—The acid (X) (0·1 g.) was distilled, to give the neutral ketone, m. p. 72°. Its 2 : 4-*dinitrophenylhydrazone* had m. p. 246° (Found: N, 15·6. $C_{19}H_{18}O_4N_4$ requires N, 15·3%) and was also obtained when the 2 : 4-dinitrophenylhydrazone of the keto-acid (X) was recrystallised from boiling ethanol. The semicarbazone formed white crystals, m. p. 233°, from ethanol. Von Braun and Reutter (*loc. cit.*) give ketone, m. p. 72°, and semicarbazone, m. p. 235°.

3a : 4 : 5 : 6-*Tetrahydroperinaphthane*-3a-*carboxylic Acid* (XI).—3*a* : 4 : 5 : 6-Tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid (0·12 g.) was reduced by the Clemmensen procedure during 1 hr. The *acid* produced was isolated in the usual way, as white needles (0·08 g.), m. p. 205—206° (from aqueous ethanol; charcoal) (Found: C, 77·7; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%).

α-2′-*Carboxyethyl*-α-*phenylglutarimide* (IV).—γ-Cyano-γ-phenylpimelonitrile (30 g.) was refluxed for 6 hr. with concentrated sulphuric acid (100 c.c.) and water (100 c.c.). The resulting solution was cooled and poured on cracked ice, and the precipitate was filtered off and recrystallised from water, to give the *imide* (24 g.) as white needles, m. p. 165° [Found: equiv., 250 (phenolphthalein); C, 64·0; H, 5·6; N, 5·3%. $C_{14}H_{15}O_4N$ requires equiv., 261; C, 64·4; H, 5·7; N, 5·4%]. The imide (10 g.), after hydrolysis with aqueous potassium hydroxide until ammonia ceased to be evolved (50 hr.), gave γ-carboxy-γ-phenylpimelic acid (8·5 g.), m. p. 153° on acidification of the reaction mixture.

1 : 2 : 3 : 4-*Tetrahydro*-4-*oxonaphthalene*-1-spiro-α-*glutarimide* (V).—α-2-Carboxyethyl-α-phenylglutarimide (10 g.) was warmed at 90° for 2 hr. with concentrated sulphuric acid (50 c.c.). The cooled mixture was poured on cracked ice, and the precipitate of *keto-imide* was filtered off and recrystallised from aqueous alcohol, to give white needles (6 g.), m. p. 198° (Found: C, 68·7; H, 5·2. $C_{14}H_{13}O_3N$ requires C, 69·1; H, 5·4%). The keto-imide was neutral to phenolphthalein but soluble in 2N-sodium hydroxide from which it was reprecipitated by hydrochloric acid. It gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 292°, as fine orange needles from glacial acetic acid (Found: N, 16·1. $C_{20}H_{17}O_6N_5$ requires N, 16·5%), and a *semicarbazone*, m. p. 258—259° (decomp.), as white needles from ethanol (Found: N, 18·3. $C_{15}H_{16}O_3N_4$ requires N, 18·7%). The imide (1·0 g.), after hydrolysis with aqueous alkali and acidification of the reaction mixture, gave 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (0·9 g.), m. p. 136° (from water).

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxonaphthalene* (VIII).—1-2′-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (0·1 g.) was decarboxylated by being heated under reflux for 5 min. The cooled semisolid acid product (VIII) was taken up in aqueous potassium hydroxide, reprecipitated by acid, and recrystallised from water; it had m. p. 106—107° (60 mg.). Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1109) gives m. p. 105—106°.

The author is indebted to Prof. S. N. Slater for suggesting the subject of the investigation and for his interest throughout its course. The work was assisted by grants for apparatus and chemicals from the Mellor Research Fund and the University of New Zealand.

UNIVERSITY OF OTAGO, DUNEDIN, NEW ZEALAND. [*Received, January 21st*, 1954.]

Cinnolines and Other Heterocyclic Types in Relation to the Chemotherapy of Trypanosomiasis. Part VIII. Attempts to Synthesise* N^1N^3*-Di-(4-amino-7-cinnolyl)guanidine Dimethiodide.*

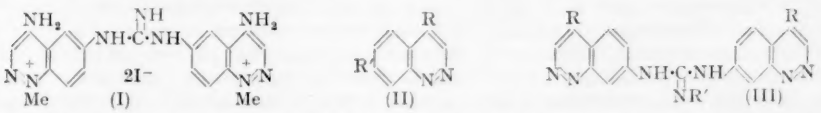
By C. M. Atkinson, (the late) J. C. E. Simpson, and A. Taylor.

[Reprint Order No. 4837.]

Attempted preparation of the compound named in the title by a method analogous to that used by Morley and Simpson (*J.*, 1952, 2617) for the synthesis of " 528 " (I) gave only a complex mixture of quaternary salts. The difficulties encountered in developing an unambiguous route to these compounds are briefly reported.

4-Hydroxy-7-nitrocinnoline (II; R = OH, R′ = NO_2) was prepared by diazotisation and cyclisation of 2-amino-4-nitroacetophenone in formic acid (McIntyre and Simpson, *J.*, 1952, 2606). Schofield and Theobald (*J.*, 1949, 2404) obtained a similar yield on a much smaller scale using acetic–sulphuric acid and a ten-fold excess of sodium nitrite. Chlorination of the hydroxy-compound and subsequent phenoxylation and amination proceeded satisfactorily on a larger scale, but a single attempt to aminate the chloro-compound (II; R = Cl, R′ = NO_2) directly with ammonia in phenol at 140° gave only a small yield of the nitro-amine (II; R = NH_2, R′ = NO_2).

Schofield and Theobald (*loc. cit.*) reported that the reduction of this compound " offered some difficulty " and were only able to isolate the diacetamido-compound (II; R = R′ = NHAc), in very low yield, after reductive acetylation. We have confirmed these results; four experiments with stannous chloride under different conditions gave unidentified high-melting material; catalytic hydrogenation proceeded beyond the reduction of the nitro-group; and the required diamine (II; R = R′ = NH_2) was finally synthesised by amination of 7-amino-4-phenoxycinnoline (II; R = OPh, R′ = NH_2). The latter derivative was prepared by the reduction of the corresponding nitro-compound with Albert and Linnell's stannous chloride–acetic anhydride reagent (*J.*, 1936, 1617). In a similar way 5- and 8-amino-4-phenoxycinnoline, required for the preparation of other isomers of " 528," were obtained.



4 : 7-Diaminocinnoline reacted with thiocarbonyl chloride, to give a sulphur-containing compound, which, on treatment with methanolic ammonia and mercuric oxide, yielded a base isomeric with that prepared by Morley and Simpson (*loc. cit.*). Quaternisation of the pure base with methyl iodide gave an amorphous salt which was shown to be a mixture of four components by paper chromatography of its aqueous solution. The mixture was inactive when tested against *T. congolense* infections in mice.

This result emphasised the importance of finding an unambiguous route to compounds of the " 528 " type. The possibility of acylation at $N_{(1)}$ and the 4-amino-group was apparent in the recovery of only 60% of 4-aminocinnoline after treatment with thiocarbonyl chloride under the conditions described by Morley and Simpson (*loc. cit.*) and in the isolation of two isomeric acetyl derivatives of the nitro-amine (II; R = NH_2, R′ = NO_2). In order to eliminate this possibility, 7-amino-4-phenoxycinnoline was treated with thiocarbonyl chloride (the phenoxy-compound was shown to be stable to the acidity which developed in the reaction under the usual conditions), but only unchanged material was isolated.

An alternative method of forming the guanidine linkage utilised dichloromethylene-benzamide Ph·CO·N:CCl_2 (Johnson and Chernoff, *J. Amer. Chem. Soc.*, 1912, **34**, 169),

* Part VII, *J.*, 1954, 165.

which with aniline or 4 : 6-diaminocinnoline gave the respective N^2-benzoyl-N^1N^3-disubstituted guanidines. However, the product from 4 : 7-diaminocinnoline methiodide and this reagent was shown by paper chromatography to be a mixture of two compounds, neither of which was the starting material.

The demonstration that 7-amino-4-phenoxycinnoline (II; R = OPh, R′ = NH_2) condensed smoothly with dichloromethylenebenzamide under the same conditions offered a means of avoiding these difficulties. The identity of the product obtained by amination and quaternisation of (III; R = OPh, R′ = Bz) with one of the products obtained from the condensation of 4 : 7-diaminocinnoline methiodide and dichloromethylenebenzamide would have fixed the position of quaternisation, and, further, there would have been no ambiguity about the position of the guanidine bridge. However, amination of the compound (III; R = OPh, R′ = Bz) gave a crystalline compound, m. p. 206—207°, the analytical figures for which precluded its representation as (III; R = NH_2, R′ = Bz).

Experimental

M. p.s were determined on a Kofler block and are corrected.

4-Hydroxy-7-nitrocinnoline.—An ice-cold solution of 2-amino-4-nitroacetophenone (Part VII, *J.*, 1954, 165; 20 g.) in formic acid (200 c.c.) was diazotised with an aqueous solution of sodium nitrite (10 g. in 50 c.c.) with stirring and external cooling. The mixture was left for 4 days at room temperature and the cinnoline, m. p. 300° (15 g.), was then collected. In experiments where gentle warming was used to assist the initial solution of the amine, the only product was *2-formamido-4-nitroacetophenone*, m. p. 155° (Found: C, 51·5; H, 3·4; N, 13·3. $C_9H_8O_4N_2$ requires C, 51·9; H, 3·8; N, 13·4%), readily hydrolysable to the amine, m. p. and mixed m. p. 166°.

7-Amino-4-phenoxycinnoline.—A stirred suspension of the nitro-compound (5 g.) (Schofield and Theobald, *loc. cit.*) in glacial acetic acid (25 c.c.) was treated with the reducing agent [125 c.c.; prepared according to Albert and Linnell (*loc. cit.*)], added during *ca.* 10 min. with external cooling to maintain the temperature at 20—25°. The complex which separated from the clear red solution towards the end of the addition was stirred for 20 min. and poured on ice (1 kg.) and aqueous sodium hydroxide (800 c.c. of 40%). The product, m. p. 178° (3·8 g., 86%), was isolated by evaporation to dryness of a washed and dried ($MgSO_4$) chloroform extract; pure *7-amino-4-phenoxycinnoline*, m. p. 179—180°, formed greenish-yellow elongated plates from benzene (Found: C, 70·5; H, 4·5; N, 17·5. $C_{14}H_9ON_3$ requires C, 70·9; H, 4·6; N, 17·75%). Attempted catalytic reduction gave no useful product although the mixture was worked up after the theoretical uptake of hydrogen (Adams catalyst in acetic acid).

4 : 7-Diaminocinnoline.—The above phenoxy-compound (0·5 g.) was added to stirred, molten ammonium acetate (5 g.) at 137° and kept at this temperature for 30 min. The clear orange solution was cooled, treated with aqueous sodium hydroxide (100 c.c.; 10%), and set aside for 4 days; the pure *diamine* (0·23 g., 76%) separated as long very pale yellow needles, m. p. 250° (decomp.) unchanged by recrystallisation from water (Found: C, 59·7; H, 5·0; N, 35·45. $C_8H_8N_4$ requires C, 60·0; H, 5·0; N, 35·0%).

N^1N^3-Di-(4-amino-7-cinnolyl)guanidine (?).—4 : 7-Diaminocinnoline (0·4 g.) was dissolved in aqueous acetone (20 c.c.; 50%) and to the hot solution thiocarbonyl chloride (0·13 c.c.) was added. The solution was stirred and refluxed for 30 min., set aside overnight, and diluted with acetone (150 c.c.), to precipitate yellow needles, m. p. 256—257° (decomp.) (0·3 g.). This material gave a positive qualitative test for sulphur and was used directly for the next stage. The above product (0·2 g.), yellow mercuric oxide (0·2 g.), and methanolic ammonia (25 c.c.; 12% w/v) were stirred together at 43—45° for 4 hr. The cooled mixture was then set aside overnight and was evaporated to dryness at room temperature. The resulting solid was broken up and extracted with hydrochloric acid (2N; 6 × 10 c.c.). The inorganic material was removed as sulphide, and the resulting mixture filtered hot. Concentration of the filtrate yielded a colourless salt which crystallised unchanged from dilute hydrochloric acid, to give *N^1N^3-di-(4-amino-7-cinnolyl)guanidine trihydrochloride* (?), m. p. 330° (decomp.) (Found: C, 41·85; H, 5·0. $C_{17}H_{15}N_9,3HCl,2H_2O$ requires C, 41·6; H, 4·5%). On dissolution in warm dilute ammonia (0·2 g. in 10 c.c.) and addition of aqueous sodium hydroxide (2 c.c.; 10%) the free base was obtained, m. p. 238—240° (0·15 g.).

Reaction between the Foregoing Guanidine and Methyl Iodide.—The base (0·1 g.) was refluxed in dry methanol (15 c.c.) for 2 hr. with methyl iodide (1 c.c.). The mixture yielded on con-

centration to dryness under reduced pressure a product, m. p. 178°, which after recrystallisation from water had m. p. 234°, with previous softening at 178° and 210° (Found: C, 34·6; H, 3·7; N, 17·45; I, 41·2. Calc. for $C_{19}H_{21}N_9I_2,2H_2O$: C, 34·3; H, 3·5; N, 18·9; I, 38·2%). Paper chromatography with a descending mixture of *tert.*-butanol (70 c.c.), 6N-hydrochloric acid (1·65 c.c.), and water (to 100 c.c.) (Atkinson and Taylor, unpublished work) showed this to be a mixture of four components, and the mother-liquors, which gave a solid, m. p. 176—178°, on evaporation to dryness, were even more complex.

Stability of 7-Nitro- and 7-Amino-4-phenoxycinnoline to Acid Hydrolysis.—Weighed samples of each compound were refluxed for 45 min. in acetone which contained dilute hydrochloric acid to make the concentration shown. In the case of the nitro-compound the percentage of unchanged material was calculated from the yield of hydroxy-compound.

Unchanged material (%).

Concentration of acid used	pH 5·91 *	N/100	N/10	N/5	N/2	N
7-Nitro-4-phenoxycinnoline	—	26·9	13·5	0	—	—
7-Amino-4-phenoxycinnoline	100	90·5	—	—	75	22

* Phosphate buffer.

Acetylation of 4-Amino-7-nitrocinnoline.—The nitro-amine (1 g.) was heated on the steam-bath with acetic anhydride (20 c.c.) for 35 min. and the hot mixture poured into water and left overnight. The crude product (0·6 g.; m. p. *ca.* 197°) gave a mixture of pale yellow needles, m. p. 234—238°, and yellow prisms, m. p. 194—196°, from alcohol. Fractional recrystallisation provided *4-acetamido-7-nitrocinnoline*, m. p. 235° (Found: C, 51·95; H, 4·3; N, 23·9. $C_{10}H_8O_3N_4$ requires C, 51·7; H, 3·45; N, 24·1%), and from the mother-liquors an isomeric *compound*, m. p. 194—195° (Found: C, 51·8; H, 4·1%).

4-Amino-7-nitrocinnoline Methiodide.—The nitro-amine (0·3 g.) (Schofield and Theobald, *loc. cit.*) was refluxed with methyl iodide (2·2 c.c.) in ethanol (7·5 c.c.) for 1½ hr.; the crude salt separated overnight. Recrystallisation from water gave orange needles of the *methiodide*, m. p. 236—238° (decomp.) (Found: C, 32·65; H, 3·0; N, 16·1; I, 37·6. $C_9H_9O_2N_4I$ requires C, 32·6; H, 2·7; N, 16·9; I, 38·2%).

4-Acetamido-7-nitrocinnoline Methiodide.—A solution of the acetamido-compound (0·35 g.; m. p. 235°) in alcohol (15 c.c.) was refluxed with methyl iodide (0·5 c.c.) for 2 hr. and the mixture was evaporated to dryness. Recrystallisation from ethanol (carbon) yielded dark red needles of *4-acetamido-7-nitrocinnoline methiodide*, m. p. 188—189° (Found: C, 35·55; H, 4·4; N, 14·25; I, 32·85. $C_{11}H_{11}O_3N_4I$ requires C, 35·3; H, 2·9; N, 14·3; I, 33·9%). Hydrolysis in boiling N-hydrochloric acid gave 4-amino-7-nitrocinnoline methiodide, m. p. 236—238° (decomp.).

4 : 7-Diaminocinnoline Methiodide.—A solution of 4-amino-7-nitrocinnoline methiodide (0·2 g.) in water (5 c.c.) was treated at 50° with a solution of stannous chloride (0·5 g.; dihydrate) in dilute hydrochloric acid (2 c.c. of water and 8 c.c. of concentrated acid). The pale yellow crystalline precipitate which separated on cooling redissolved at 65° and after 20 min. at this temperature the mixture was cooled, giving a colourless precipitate. After 1 hr. at room temperature the mixture was diluted with water and freed from tin salts with hydrogen sulphide, and the filtrate was evaporated (desiccator) to a black dry solid. This was dissolved in boiling water (charcoal), and the methiodide precipitated with saturated aqueous potassium iodide. *4 : 7-Diaminocinnoline methiodide* formed long yellow needles, m. p. 262—263° (0·1 g.), from ethanol (Found: C, 36·25; H, 4·2; N, 18·4. $C_9H_{11}N_4I$ requires C, 35·85; H, 3·6; N, 18·5%).

Dichloromethylenebenzamide (Johnson and Chernoff, *loc. cit.*).—Potassium thiocyanate (25 g.) in water (50 c.c.) was treated with a filtered solution of lead acetate (55 g.) in water (200 c.c.). The heavy white precipitate was filtered off, washed twice with water, then with ethanol, and dried in a desiccator over concentrated sulphuric acid (yield, 27 g.). Lead thiocyanate (54 g.) and benzoyl chloride (45 g.) in dry benzene were stirred at reflux temperature (88°) for 1 hr., the solvent was removed after filtration, and benzoyl thiocyanate (34·3 g.; 62%) distilled off (b. p. 104°/0·5 mm.). Dry chlorine was passed through a solution of benzoyl thiocyanate (34 g.) in anhydrous carbon tetrachloride (110 c.c.) for 4 hr. The mixture was filtered after 66 hr., the sulphur chloride and carbon tetrachloride were removed at slightly reduced pressure, and the residue was distilled (b. p. 119—120°/15 mm.). The pale yellow product (36·2 g.) was redistilled, giving dichloromethylenebenzamide, a stable colourless liquid, b. p. 79°/0·5 mm., n_{15}^{D} 1·5675 (27·15 g., 61%).

N^1N^3-*Di*-(4-*amino*-6-*cinnolyl*)*guanidine*.—A stirred suspension of 4 : 6-diaminocinnoline (0·3 g.) (*J.*, 1952, 2597) in nitromethane (25 c.c.) was treated at *ca.* 5° with a solution of dichloromethylenebenzamide (0·3 c.c.) in nitromethane (5 c.c.). After 3½ hr. the red precipitate (0·35 g.) was filtered off and dried, and the finely divided solid was stirred with dilute aqueous ammonia, to give a yellow base. This (0·1 g.) was refluxed for 2 hr. with alcoholic potassium hydroxide (0·5 g. in 30 c.c.), then concentrated under reduced pressure, and the residue was washed with water and dried at 70°. The product (0·06 g.), m. p. 250—255°, was dissolved in dilute hydrochloric acid (charcoal), filtered, and further acidified with concentrated hydrochloric acid. Colourless fibrous needles were obtained on seeding with the authentic guanidine (Morley and Simpson, *loc. cit.*), which showed the same solubility and m. p. characteristics.

N^2-*Benzoyl*-N^1N^3-*di*-(4-*phenoxy*-7-*cinnolyl*)*guanidine*.—To 7-amino-4-phenoxycinnoline (0·1 g.) in nitromethane (5 c.c.), dichloromethylenebenzamide (0·1 g.) in nitromethane (2 c.c.) was added. An orange solid, m. p. >350° (0·15 g., average for 6 experiments), which was slowly precipitated, was collected after 1½ hr. at room temperature. The guanidine, m. p. >350°, crystallised from nitromethane in very low yield as the *trihydrochloride* (Found : C, 61·1; H, 4·5. $C_{36}H_{25}O_3N_7$,3HCl requires C, 61·0; H, 4·0%). Passage of dry ammonia through a suspension of the salt in nitromethane gave a white base, m. p. 240—242°. This crystallised (with poor recovery) from Cellosolve (2-ethoxyethanol) as colourless needles, m. p. 244—245°.

Reaction of the Preceding Guanidine with Ammonium Acetate.—The guanidine (0·7 g.) was added to molten ammonium acetate (20 g.) at 135° and the temperature raised to 160° and kept thereat, with occasional stirring, for ½ hr. The clear solution which was obtained after 10 min. was cooled, poured into aqueous sodium hydroxide (10%; 30 c.c.), and, next morning, the crystalline precipitate (0·13 g.), m. p. 204—205°, was collected. This *compound* formed colourless blades, m. p. 206—207°, from ethanol (Found : C, 61·3; H, 4·5; N, 16·8%). A derivative, $C_{24}H_{19}ON_9,H_2O$, of (III) requires C, 61·6; H, 4·5; N, 27·0%.

8-*Amino*-4-*phenoxycinnoline*.—8-Nitro-4-phenoxycinnoline (2·8 g.) (Schofield and Theobald, *loc. cit.*) was suspended in glacial acetic acid (5 c.c.), and frozen at 15°. This solid was treated with Albert and Linnell's reagent (*loc. cit.*) (100 c.c.) at >15°. An almost colourless solid separated from the deep maroon solution which was formed initially, and the mixture was kept for ½ hr. at 10°, then poured on to ice (500 g.) and aqueous sodium hydroxide (250 c.c.; 40%). The product which separated was extracted with chloroform, and evaporation of the washed and dried ($MgSO_4$) extract yielded a crude product, m. p. 128—129° (2·1 g.). 8-*Amino*-4-*phenoxycinnoline*, b. p. 130°, separated from benzene–light petroleum (b. p. 60—80°; 1 : 1, v/v) in rhombs, m. p. 130° (Found : C, 71·35; H, 4·75; N, 17·6. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·75%).

5-*Amino*-4-*phenoxycinnoline*.—4-Chloro-5-nitrocinnoline (0·5 g.; Schofield and Theobald, *loc. cit.*), ammonium carbonate (2 g.), and phenol (50 g.) were rapidly ground together and then heated on a steam-bath for ½ hr. The mixture was diluted with water and treated with 40% aqueous sodium hydroxide (120 c.c.), and the resulting solution extracted with chloroform. The washed and dried extract was evaporated to dryness (0·6 g.), and the residue was recrystallised from light petroleum (b. p. 40—60; 50 c.c.)–benzene (2 c.c.) (charcoal), to provide long very pale green needles, m. p. 114—115°. Further recrystallisation (as before) gave needles, m. p. 122—123°. 5-*Nitro*-4-*phenoxycinnoline* separated from light petroleum (b. p. 40—60°) in almost colourless needles, m. p. 123° (Found : C, 62·4; H, 3·8. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4%). The product (0·15 g.; m. p. 122—123°) was suspended in glacial acetic acid (1 c.c.) and treated at 10° with the reagent (3·5 c.c.; Albert and Linnell, *loc. cit.*). An almost colourless precipitate separated immediately and the mixture was gently shaken for 20 min. and poured into 40% aqueous sodium hydroxide (100 c.c.) and ice (100 g.). Evaporation of a washed and dried ($MgSO_4$) chloroform extract gave a residue which yielded, on cooling of a filtered benzene digest and further crystallisation from benzene, pure 5-*amino*-4-*phenoxycinnoline* as yellow needles, m. p. 199—200° (decomp.) (0·08 g., 79%) (Found : C, 70·65; H, 4·4; N, 17·6. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·75%).

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Medical Research Council Group for Research in Chemotherapy,
University of Manchester.
Department of Chemistry, Chelsea Polytechnic. [*Received, November 26th*, 1953.]

Hydrazine. Part VII. Some Halogeno-antimonites and -bismuthites of Hydrazine.*

By W. Pugh.

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The following new complexes have been prepared by crystallisation, from aqueous solutions, of mixtures of antimony or bismuth halide and the corresponding hydrazine halide:† $(N_2H_5)_2SbCl_5$; $(N_2H_5)_2BiCl_5$; $N_2H_5HBiCl_5,2H_2O$; $N_2H_5BiCl_4$; $(N_2H_5)_{11}Sb_2Br_{17}$; $(N_2H_5)_{10}Sb_3Br_{19}$; $(N_2H_5)_2SbBr_5$; $(N_2H_5)_3Sb_2Br_9$; $(N_2H_5)_4BiBr_7$; $(N_2H_5)_3BiBr_6$; $(N_2H_5)_6HBi_3Br_{16},10H_2O$; $N_2H_5HBiBr_5,4H_2O$; $(N_2H_5)_3Bi_2Br_9$; $(N_2H_5)_3SbI_6$; $N_2H_5SbI_4,3H_2O$; $(N_2H_5)_3BiI_6$; $(N_2H_5)_5Bi_3I_{14},6H_2O$; $(N_2H_5)_6HBi_4I_{19},10H_2O$. The chloro-complexes are colourless, the bromo- yellow, and the iodo- red; they are very soluble in water, forming colourless, yellow, or red solutions which are decomposed on dilution, giving insoluble basic antimony or bismuth halides.

Antimony and bismuth seem to form a great variety of complex halides, ranging in composition from the simpler ones, *e.g.*, $NaSbI_4$, K_2SbCl_5, and K_3BiCl_6, to highly complex ones, *e.g.*, $(NH_4)_7Sb_3Br_{16}$ and $(NH_4)_3Sb_4I_{15},9H_2O$ (Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans Green and Co., London, 1929, Vol. IX, pp. 479, 496, 502, 666, 672, 676). Some highly complex iodoantimonites of some ketazines have recently been reported in Part VI (*loc. cit.*). However, the only complex halides of these metals with the hydrazinium cation, so far described, are the fluoro-salts (Part III, *loc. cit.*), and the hexachloroantimonite and the hexachlorobismuthite prepared by Ferratini (*Gazzetta*, 1912, **42**, 138) by boiling the metal chlorides in alcoholic solution with solid hydrazine hydrochloride.

The present paper confirms the individualities of these two chloro-salts (which, however, have now been obtained from aqueous solutions) and also describes a number of other complex antimonites and bismuthites which are no less remarkable for their variety and complexity. The new compounds are formulated in the summary. These salts were all made by crystallisation from aqueous solution, though better results were obtained from aqueous-alcoholic solution in a few cases; but no claim is made that the above is an exhaustive list of all possible compounds. The experimental details given later show that the composition of the solid phase, at room temperature, depends not only on the weight ratio of the component simple salts but also on the concentration of free halogen acid. Phase-rule studies would no doubt establish the existence of other compounds in these series.

The chloro-salts are colourless, the bromo-salts yellow, and the iodo-salts red. They are all exceedingly soluble in water, and deliquescent; most of them dissolve in a fraction of their own weight of water, forming colourless, yellow, or red solutions, which are decomposed on dilution, with separation of insoluble basic salts. They are insoluble in light petroleum, benzene, carbon tetrachloride, chloroform, ether, and alcohol (except the iodo-salts which are soluble in alcohol), but they dissolve readily in acetone–water, forming the corresponding salts of dimethylketazine (Part VI, *loc. cit.*).

Experimental

The methods of analysis used have been described in Part VI (*loc. cit.*). In this section complexes are named for convenience as salts of complex ions without prejudice as to the actual existence of the complex ions implied.

* Parts III, VI, *J.*, 1953, 1934, 3445.

† These formulæ are given for simplicity, but with full realisation that some of the compounds, at least, may be double salts or lattice compounds rather than complex ions. Only structure investigations can determine the exact co-ordination number of the metals in the compounds.

General Method of Preparation.—The chloro- and bromo-salts were prepared from antimony and bismuth trioxides and hydrazine hydrate as source materials. Solutions of the metal oxides in concentrated hydrochloric, or hydrobromic, acid were treated with the appropriate quantities of hydrazine hydrochloride, or hydrobromide, solution, prepared by neutralising hydrazine hydrate (60%) with concentrated acid (methyl-orange indicator). Crystallisation was at room temperature, by slow evaporation in air or, sometimes, over desiccating agents. In some cases, indicated below, the metal halide solution was evaporated to dryness, or as near dryness as possible, to remove excess of acid, before the hydrazine salt solution was added. It was from solutions which had not been so evaporated that the acid salts described separated.

The iodo-salts were prepared by dissolving antimony tri-iodide and bismuth iodide in warm solutions of hydrazine hydriodide, but addition of free hydrioidic acid was found necessary when the formal ratio was less than 3 : 1.

Whenever any of the mixed solutions were boiled, separation of metallic antimony or bismuth occurred, with evolution of nitrogen; however, it was always possible to concentrate the solutions on the water-bath, because reduction was seldom noticeable at this temperature; cold solutions generally remained stable indefinitely.

In the various preparations described, the term "formal ratio" means the number of formula weights of hydrazine salt per formula weight of metal halide.

The Chloroantimonites.—(a) *Trihydrazinium hexachloroantimonite.* Hydrazine monohydrochloride and antimony trichloride, formal ratio 3 : 1, were dissolved in half their combined weight of water. The solution effervesced slowly (nitrogen) and deposited antimony during several hours. However, rapid evaporation under reduced pressure yielded colourless, silky needles, m. p. 138—140°, free from metallic antimony (dried *in vacuo*; H_2SO_4) [Found: N_2H_4, 21·9; Cl, 49·0; Sb, 27·9. Calc. for $(N_2H_5)_3SbCl_6$: N_2H_4, 22·1; Cl, 49·1; Sb, 28·1%]. A less pure product was obtained by boiling under reflux for 4 hr. a chloroform solution of antimony trichloride, in large excess, with solid hydrazine monohydrochloride. The latter slowly changed its form and appearance, and the yield was nearly quantitative.

(b) *Dihydrazinium pentachloroantimonite.* Antimony trichloride dissolved in a concentrated solution of hydrazine dihydrochloride (formal ratio 2 : 1), but slow evaporation of the solution led to continuous separation of hydrazine dihydrochloride. The *pentachloro*-salt was made from a mixture of the above salts (formal ratio 1 : 1) by evaporation with hydrochloric acid, on the water-bath, to a syrupy consistency, the syrup then being shaken with its own volume of ethanol. (Hydrazine dihydrochloride again separated but redissolved as evaporation proceeded.) The mixture slowly separated into two phases, and the lower phase yielded colourless needles at 0° [Found, on crystals dried *in vacuo*: N_2H_4, 17·5; Cl, 48·5; Sb, 33·2. $(N_2H_5)_2SbCl_5$ requires N_2H_4, 17·5; Cl, 48·5; Sb, 33·4%].

The Chlorobismuthites.—(a) *Trihydrazinium hexachlorobismuthite.* Hot concentrated solutions of hydrazine dihydrochloride dissolve bismuth trioxide, and a solution of the mixed chlorides, formal ratio 3 : 1, was made in this way. Evaporation over desiccating agents then yielded the hexachlorobismuthite as long, flat prisms and plates, often with domed ends [Found, on material dried *in vacuo*: N_2H_4, 18·4; Cl, 40·8; Bi, 40·2. Calc. for $(N_2H_5)_3BiCl_6$: N_2H_4, 18·4; Cl, 40·9; Bi, 40·1%]. (The same compound was precipitated from the mother-liquors by addition of ethanol). The crystals melt partially at 210° but there is evidence of slow decomposition (gas evolution) at temperatures as low as 120°; gas evolution is vigorous at the m. p.

(b) *Dihydrazinium pentachlorobismuthite.* This *chlorobismuthite* was obtained as fine colourless needles from a highly concentrated, acid-free, solution of the mixed chlorides, formal ratio 2 : 1 (prepared by evaporating bismuth oxide with excess of hydrochloric acid to complete dryness, and dissolving the acid-free chloride in hydrazine monohydrochloride solution) [Found, on material dried *in vacuo*: N_2H_4, 14·1; Cl, 39·2; Bi, 46·3. $(N_2H_5)_2BiCl_5$ requires N_2H_4, 14·2; Cl, 39·2; Bi, 46·2%]. This salt also shows signs of decomposition at temperatures below its m. p. (190—195°) and it decomposes actively over the melting range.

(c) *Hydrazinium hydrogen pentachlorobismuthite and* (d) *hydrazinium tetrachlorobismuthite.* These two salts were obtained by crystallisation of mixtures, formal ratio 2 : 1, containing free hydrochloric acid. The first crops consisted of colourless needles, or plates with domed ends, of the acid pentachlorobismuthite as a *dihydrate* [Found: N_2H_4, 7·2; Cl, 38·9; Bi, 46·2. $N_2H_5HBiCl_5,2H_2O$ requires N_2H_4, 7·0; Cl, 39·0; Bi, 45·8%]. The middle fractions were mixtures of this salt and the *tetrachlorobismuthite*, which in turn was the sole constituent of the tail fractions (colourless needles) [Found: N_2H_4, 7·9; Cl, 37·0; Bi, 54·6. $N_2H_5BiCl_4$ requires N_2H_4, 8·3; Cl, 37·0; Bi, 54·5%].

The Bromoantimonites.—(a) *Undecahydrazinium heptadecabromodiantimonite.* A mixed solution of hydrazine hydrobromide and antimony tribromide (formal ratio 3 : 1) was used, the solution of antimony oxide in hydrobromic acid having been evaporated to near-dryness on the water-bath before addition of the hydrazine salt solution. The mixed warm solution was then treated with an equal volume of methanol, and yellow, granular crystals of the *heptadecabromo-*salt separated [Found: N_2H_4, 18·2; Br, 69·4; Sb, 12·4. $(N_2H_5)_{11}Sb_2Br_{17}$ requires N_2H_4, 18·3; Br, 69·2; Sb, 12·4%]. The crystals melt partially at 165°, clearing at 186°, but there is considerable gas evolution at intermediate temperatures, and decomposition is vigorous at 186°. Crystallisation of similar mixtures from hydrobromic acid solutions (without preliminary evaporation) yielded mixtures of the above salt and the nonabromodiantimonite described below under (d).

(b) *Decahydrazinium nonadecabromotriantimonite.* Mixtures, of formal ratio 3 : 1, crystallised from aqueous solution free from excess of hydrobromic acid, yielded a number of products. The first fractions consisted essentially of the heptadecabromo-salt (a); the middle fractions approximated closely in composition to trihydrazinium hexabromoantimonite, but this salt was not obtained pure; the last fractions consisted of long, slender, yellow needles of *decahydrazinium nonadecabromotriantimonite* [Found: N_2H_4, 14·4; Br, 68·4; Sb, 16·5. $(N_2H_5)_{10}Sb_3Br_{19}$ requires N_2H_4, 14·4; Br, 68·6; Sb, 16·5%].

(c) *Dihydrazinium pentabromoantimonite.* The earlier fractions obtained by crystallising mixtures of formal ratio 2 : 1, containing the minimum of hydrobromic acid, consisted of granular yellow crystals of the *pentabromoantimonite* [Found: N_2H_4, 10·7; Br, 67·5; Sb, 20·4. $(N_2H_5)_2SbBr_5$ requires N_2H_4, 10·9; Br, 68·0; Sb, 20·7%].

(d) *Trihydrazinium nonabromodiantimonite.* The middle fractions obtained in the immediately preceding preparation (c) consisted of the pure *nonabromodiantimonite*, but this salt was obtained more easily from a mixture of formal ratio 1 : 1, prepared by evaporating antimony oxide with hydrobromic acid to near-dryness and adding a concentrated solution of hydrazine monohydrobromide. It separated as yellow blades and plates which are not deliquescent in dry weather [Found: N_2H_4, 8·9; Br, 67·6; Sb, 22·9. $(N_2H_5)_3Sb_2Br_9$ requires N_2H_4, 9·0; Br, 67·7; Sb, 22·9%].

The Bromobismuthites.—(a) *Tetrahydrazinium heptabromobismuthite.* Concentrated solutions of mixtures of hydrazine and bismuth bromides, formal ratio 3 : 1, which are free from hydrobromic acid, undergo slow decomposition, even when cold. They become dark and deposit bismuth slowly. The first two crystal fractions obtained by evaporating such solutions over calcium chloride were essentially the *heptabromobismuthite*, as yellow needles and laths, contaminated with bismuth inclusions [Found: N_2H_4, 13·8; Br, 61·3; Bi, 24·3. $(N_2H_5)_4BiBr_7$ requires N_2H_4, 14·2; Br, 62·2; Bi, 23·2%].

(b) *Trihydrazinium hexabromobismuthite.* Following the above crops of the heptabromo-salt, there appeared several crops of yellow rhomboidal bars or needles of the *hexabromobismuthite.* However, this salt was obtained more easily, in better yields, and without separation of bismuth by treating a similar mixture (formal ratio 3 : 1), containing free hydrobromic acid, with its own volume of ethanol, and cooling it to 0° [Found: N_2H_4, 12·2; Br, 60·8; Bi, 26·5. $(N_2H_5)_3BiBr_6$ requires N_2H_4, 12·2; Br, 61·0; Bi, 26·6%]. The salt does not melt; it decomposes actively at 215° (approx.).

(c) *Hexahydrazinium hydrogen hexadecabromotribismuthite.* This salt separated as the *decahydrate*, in large, tetragonal, yellow prisms, or flat oblong tablets, from mixed solutions of hydrazine and bismuth bromides (formal ratio 2 : 1), which were free from hydrobromic acid [Found: N_2H_4, 8·5; Br, 56·1; Bi, 27·5; H_2O, 8·0. $(N_2H_5)_6HBi_3Br_{16},10H_2O$ requires N_2H_4, 8·4; Br, 56·0; Bi, 27·4; H_2O, 7·9%]. The hydrated salt dissolves partially in its water of hydration at 48°, and completely at 80°. It loses its water of hydration very readily, desiccation *in vacuo* over sulphuric acid at 20° yielding the anhydrous *salt* [Found: N_2H_4, 9·1; Br, 61·0; Bi, 29·6. $(N_2H_5)_6HBi_3Br_{16}$ requires N_2H_4, 9·1; Br, 61·0; Bi, 29·7%].

(d) *Trihydrazinium nonabromodibismuthite.* Mixed solutions of the simple salts, of formal ratio 1·5 : 1 and free from hydrobromic acid, yielded the pure *nonabromodibismuthite* as yellow needles and prisms [Found, on material dried *in vacuo*: N_2H_4, 7·7; Br, 58·3; Bi, 33·6. $(N_2H_5)_3Bi_2Br_9$ requires N_2H_4, 7·8; Br, 58·2; Bi, 33·8%].

(e) *Hydrazinium hydrogen pentabromobismuthite.* The pure *tetrahydrate* of this salt was obtained in the later fractions which separated from mixtures (formal ratio 1 : 1) dissolved in hydrobromic acid [Found: N_2H_4, 4·5; Br, 55·8; Bi, 29·1. $N_2H_5HBiBr_5,4H_2O$ requires N_2H_4, 4·5; Br, 55·9; Bi, 29·2%]. [The earlier fractions were mixtures of this salt and the nonabromodibismuthite (d).] It forms yellow needles and prisms which are very deliquescent, and lose

water rapidly (approx. 4 mols.) over sulphuric acid. This initial rapid loss is followed by a slower loss of hydrogen bromide.

The Iodoantimonites.—(a) *Trihydrazinium hexaiodoantimonite.* Antimony tri-iodide dissolved completely in aqueous solutions of hydrazine hydriodide, provided the formal ratio was 3 : 1, and the dark red solutions yielded scarlet needles and prisms of the *hexaiodoantimonite* [Found: N_2H_4, 9·8; I, 77·8; Sb, 12·4. $(N_2H_5)_3SbI_6$ requires N_2H_4, 9·8; I, 77·5; Sb, 12·4%].

(b) *Hydrazinium tetraiodoantimonite.* Antimony tri-iodide was dissolved in hot aqueous hydrazine hydriodide solution (formal ratio 1 : 1) with the aid of the minimum amount of hydriodic acid, the red solution depositing dark red, almost black, octahedra of the tetraiodoantimonite as *trihydrate* (Found: N_2H_4, 4·4; I, 71·5; Sb, 17·0; H_2O, 7·8. $N_2H_5SbI_4,3H_2O$ requires N_2H_4, 4·5; I, 71·0; Sb, 17·0; H_2O, 7·5%). The *anhydrous* salt was obtained as a maroon powder by desiccating the above hydrate over sulphuric acid (Found: N_2H_4, 4·7; I, 77·0; Sb, 18·4. $N_2H_5SbI_4$ requires N_2H_4, 4·8; I, 76·6; Sb, 18·4%).

The Iodobismuthites.—(a) *Trihydrazinium hexaiodobismuthite.* The dark red aqueous solutions containing hydrazine hydriodide and bismuth iodide (formal ratio 3 : 1) yielded scarlet needles and tetragonal prisms of the *hexaiodobismuthite*, m. p. 182° (decomp. with vigorous gas evolution) [Found: N_2H_4, 9·0; I, 71·2; Bi, 19·7. $(N_2H_5)_3BiI_6$ requires N_2H_4, 9·0; I, 71·2; Bi, 19·6%].

(b) *Pentahydrazinium tetradecaiodotribismuthite.* Mixtures of the simple iodides of formal ratio 2 : 1 and 1·5 : 1, containing the minimum of free hydriodic acid for complete solution, did not yield the expected pentaiodo-salt or the iodo-analogues of the bromo-salts (see above) obtained from similar mixtures; instead, they yielded pentahydrazinium tetradecaiodotribismuthite as the *hexahydrate*, ruby-red needles and elongated prisms and plates [Found: N_2H_4, 5·9; I, 66·3; Bi, 23·4; H_2O, 4·3. $(N_2H_5)_5Bi_3I_{14},6H_2O$ requires N_2H_4, 6·0; I, 66·5; Bi, 23·4; H_2O, 4·1%]. The hydrated salt loses its water of crystallisation readily over sulphuric acid, yielding black lustrous crystals of the *anhydrous* salt [Found: N_2H_4, 6·2; I, 69·3; Bi, 24·4. $(N_2H_5)_5Bi_3I_{14}$ requires N_2H_4, 6·2; I, 69·2; Bi, 24·4%].

(c) *Hexahydrazinium hydrogen nonadecaiodotetrabismuthite.* Mixtures of formal ratio 1 : 1 in hydriodic acid solution yielded the *decahydrate* of this salt as dark red needles, m. p. 75° [Found: N_2H_4, 5·2; I, 65·8; Bi, 22·8; H_2O, 6·0. $(N_2H_5)_6HBi_4I_{19},10H_2O$ requires N_2H_4, 5·2; I, 66·0; Bi, 22·8; H_2O, 5·9%]. It loses its water of crystallisation when kept over sulphuric acid, but there is a slight loss of hydrogen iodide at the same time.

Acknowledgment is made to the University Council for grants from the Staff Research Fund for materials used in this series of investigations.

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The Chemistry of Plant Growth-regulators. Part II. Modification of the Side-chain of 2 : 4-Dichlorophenoxyacetic Acid.*

By G. W. K. CAVILL and D. L. FORD.

[Reprint Order No. 4929.]

The synthesis of some 2 : 4-dichlorophenoxyacetic acids modified in the side-chain and related benzo-1 : 3-dioxole-2-carboxylic acids is described. Growth-regulating properties of these compounds are briefly discussed.

IT was concluded in Part I * that hydroxylation of 2 : 4-dichlorophenoxyacetic acid (2 : 4-D) in the 6-position is not a metabolic process essential before growth-regulating properties are shown. Hypotheses relating plant growth-regulating activity with the structure of the aryloxyalkanecarboxylic acids, recently reviewed by Wain ("Plant Growth Substances," Roy. Inst. Chem., London, 1953), have stressed that the $-O\cdot CH\cdot CO_2H$ system is essential and, further, have considered the significance of the configuration of the carbon atom α to the carboxyl group. Some phenoxyacetic acids modified in the side-chain have now been synthesised to test such relations.

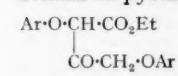
Previous investigations of the phenoxy-acids of the type $ArO\cdot CHR\cdot CO_2H$ have been

* Part I, *J.*, 1954, 565.

confined to those compounds in which R is an alkyl or aryl group (cf. Wain, *op. cit.*) and we now report the introduction of acyl and ester substituents into the α-position.

2 : 4-Dichlorophenoxymalonic acid has been synthesised but exhibits low growth-regulating activity. Such relative inactivity in a system which is readily decarboxylated by chemical processes to a phenoxyacetic acid, was unexpected; however, significant activity is shown in the following α-(2 : 4-dichlorophenoxy)-β-oxo-esters.

Claisen condensation of ethyl 2 : 4-dichlorophenoxyacetate with ethyl oxalate proceeded normally in ether, yielding ethyl 2 : 4-dichlorophenoxyoxaloacetate, which was isolated and purified as the copper salt (cf. Huntress and Olsen, *J. Amer. Chem. Soc.*, 1948, **70**, 2856, for parent compound). Self-condensation of ethyl 2 : 4-dichlorophenoxyacetate occurs in toluene and the sodio-derivative of ethyl αγ-bis-(2 : 4-dichlorophenoxyacetoacetate is precipitated. This salt has unusual properties, being insoluble in water and ethyl alcohol, soluble in pyridine and hot nitrobenzene, and unaffected by cold dilute hydrochloric acid. The parent ester can be obtained by the action of hot acetic acid on the sodio-derivative, which is reprecipitated on titration with alcoholic sodium hydroxide solution (phenolphthalein). Hydrolysis with alcoholic potassium hydroxide to 2 mols. of the 2 : 4-dichlorophenoxyacetic acid confirms the structure (inset).



Some benzo-1 : 3-dioxole-2-carboxylic acids have been prepared for comparison with the corresponding phenoxyacetic acids. First, in the benzodioxole system the carboxyl group is held in a fixed position to the plane of the ring and, secondly, if activity is present in some nuclear chlorinated derivatives, then resolution of such compounds would yield information on the effect of the configuration of the α-carbon atom. A low yield in the synthesis of the parent benzo-1 : 3-dioxole-2-carboxylic acid from catechol, sodium, and ethyl dichloroacetate was noted by Burger, Markees, Nes, and Yost (*ibid.*, 1949, **71**, 3307) and we have improved the yield (to 23%) by the use of a continuous-extraction process. 5-Chloro- and 4 : 6-dichloro-benzo-1 : 3-dioxole-2-carboxylic acids were also readily isolated by this method. Direct chlorination of the parent acid yielded a (?5 : 6-)dichloro-derivative. Several alternative syntheses were unsuccessfully attempted. 2 : 2-Di-alkylbenzo-1 : 3-dioxoles were obtained in good yield by condensation of catechol with ketones in the presence of phosphoric oxide (Sloof, *Rec. Trav. chim.*, 1935, **54**, 995). We confirmed this procedure, for example, in the synthesis of 2 : 2-di*iso*butylbenzo-1 : 3-dioxole, but were unable to oxidise such alkyl derivatives to the carboxylic acids. Further investigations of the dioxoles were abandoned when preliminary testing of the 5-chloro-acid showed no growth-regulating activity. Rather, such results support Wain's hypothesis (*op. cit.*) of free rotation of the oxyacetate moiety.

We also synthesised *meso*-αα′-bis-2 : 4-dichlorophenoxysuccinic acid and ethyl 2 : 4-dichlorophenyl oxalate. The former, which retains the $\cdot O\cdot CH\cdot CO_2H$ grouping, might result by dehydrogenation and the latter by direct oxidation of 2 : 4-dichlorophenoxyacetic acid in the plant. Neither of these compounds showed activity. Finally, 2 : 4-dichloro-phenoxyacetone has been synthesised and its lack of growth-regulating activity shows that the acid carboxyl and not the polar carbonyl group is an essential feature.

The preliminary testing procedure employed was that of effect on the elongation of the primary maize root, and the results reported above are in general agreement with current correlations between structure and activity in the aryloxyalkanecarboxylic acids. There is considerable specificity in the constitution of the single substituent allowable on the α-carbon atom. The order of inhibitive activity is 2 : 4 : 1-$C_6H_3Cl_2\cdot O\cdot CH_2\cdot CO_2H \gg$ ethyl αγ-bis-2 : 4-dichlorophenoxyacetoacetate $>$ 2 : 4 : 1-$C_6H_3Cl_2\cdot O\cdot CH(CO_2H)_2$. The series showing high activity in this investigation is the β-keto-esters, and their enolic salts and chelate derivatives. The insolubility and non-volatility of the sodio-salt of the aceto-acetate and its ability to yield 2 : 4-dichlorophenoxyacetic acid on alkaline hydrolysis might lead to useful practical applications.

Experimental

2 : 4-*Dichlorophenoxymalonic Acid.*—Ethyl chloromalonate (19·5 g.) was added to a hot solution of sodium 2 : 4-dichlorophenoxide [from the dichlorophenol (16·3 g.) and sodium (2·3 g.)] in ethanol (100 ml.), and the mixture heated at reflux for 2 hr. Ethyl 2 : 4-dichloro-

phenoxymalonate, isolated by ether-extraction, was a colourless oil, b. p. 164—167°/2·0 mm. (slight decomp.). The crude ester was hydrolysed with excess of alcoholic potassium hydroxide solution, and the acid separated (21·5 g.), m. p. 142—144° (decomp.), on acidification. Recrystallisation from benzene–ether gave 2 : 4-*dichlorophenoxymalonic acid* (12·0 g.) as colourless needles with bitter taste and m. p. 148—149° (decomp.; inserted in bath at 146°) (Found: C, 41·0; H, 2·4. $C_9H_6O_5Cl_2$ requires C, 40·8; H, 2·3%). The acid, which is decarboxylated at the m. p., solidifies on cooling and remelts at 138° (mixed m. p. with 2 : 4-dichlorophenoxyacetic acid, m. p. 140°, is not depressed).

Ethyl 2 : 4-*Dichlorophenoxyoxaloacetate*.—This ester (170 g.), prepared from ethyl 2 : 4-dichlorophenoxyacetate (124·5 g.) and ethyl oxalate (80·3 g.) by Huntress and Olsen's method (*loc. cit.*), was a pale yellow viscous oil, soluble in dilute sodium hydroxide solution and giving a deep red colour with alcoholic ferric chloride. A *copper* derivative, prepared from the oxaloacetate (17·45 g.) in alcohol (50 ml.) with crystalline copper sulphate (8·0 g.) and sodium acetate trihydrate (8·0 g.) in water (60 ml.), was precipitated as an apple-green powder; it recrystallised from alcohol as long green needles (16·0 g.), m. p. 205°, with a reversible brown (hot)–green (cold) colour change (Found: C, 44·5; H, 3·4. $C_{28}H_{26}O_{12}Cl_4Cu$ requires C, 44·3; H, 3·5%). It is insoluble in water and light petroleum, sparingly soluble in ether, but soluble in chloroform, benzene, and acetone. Hydrolysis of the copper derivative with cold hydrochloric acid (5N) under ether yields *ethyl* 2 : 4-*dichlorophenoxyoxaloacetate*, with slight decomposition, as a pale-yellow viscous oil, $d_D^{23·5}$ 1·318, $n_D^{23·5}$ 1·5243 (Found: C, 46·1; H, 4·2. $C_{14}H_{14}O_6Cl_2$ requires C, 48·1; H, 4·0%). Better analytical figures cannot be obtained owing to partial hydrolysis; the product re-forms the copper derivative in >90% yield.

Ethyl αγ-Bis-2 : 4-*dichlorophenoxyacetoacetate*.—Addition of ethyl 2 : 4-dichlorophenoxyacetate (124·5 g.) to a hot solution of ethyl oxalate (80·3 g., 10% excess) and sodium ethoxide (from 11·5 g. of sodium) in toluene (100 ml.) caused rapid precipitation of a colourless salt. The reaction was forced, during 5 hr., by distillation of the ethanol–toluene azeotrope from the mixture, the theoretical quantity of ethanol (46 g.) being recovered. The dried insoluble *sodio*-derivative (73 g.), isolated after washing with toluene and water, crystallised from pyridine as small colourless prisms (Found: C, 45·5; H, 2·8; Cl, 29·5; Na, 4·7. $C_{18}H_{13}O_5Cl_4Na$ requires C, 45·6; H, 2·8; Cl, 29·9; Na, 4·9%). It gave a deep purple colour with neutral ferric chloride solution.

The sodio-compound (50 g.) was added to hot acetic acid (200 ml.) and, on cooling, *ethyl αγ-bis*-2 : 4-*dichlorophenoxyacetoacetate* crystallised as slender colourless needles, m. p. 99°, in almost theoretical yield [Found: C, 47·5; H, 3·3%; *M* (Rast), 446. $C_{18}H_{14}O_5Cl_4$ requires C, 47·8; H, 3·1%; *M*, 452].

Hydrolysis of the ester (11·0 g.) with excess of alcoholic potassium hydroxide gave 2 : 4-dichlorophenoxyacetic acid as colourless prisms (8·5 g., 97%), m. p. and mixed m. p. 141°. No carbon dioxide or oxalate ion was found.

Benzo-1 : 3-*dioxole*-2-*carboxylic Acid and its Chloro-derivatives*.—Catechol (11 g.) in butanol (20 ml.) was heated with hot sodium butoxide solution [from sodium (4·6 g.) in butanol (100 ml.)] under reflux in an atmosphere of hydrogen; a colourless sodium salt was precipitated. Butyl dichloroacetate (18·5 g.) was added during 10 min. Titration with standard hydrochloric acid (methyl-orange) showed 83% reaction in 1 hr. and 92·5% in 2 hr. The mixture, after hydrolysis with aqueous sodium hydroxide solution and steam-distillation to remove butanol, on acidification, yielded an acidic black polymeric oil. Continuous extraction of this product with light petroleum gave the benzo-1 : 3-dioxole-2-carboxylic acid (3·8 g.) as large colourless plates, m. p. 109° (Found: C, 57·7; H, 3·6. Calc. for $C_8H_6O_4$: C, 57·8; H, 3·6%). Burger *et al.* (*loc. cit.*) record m. p. 104—106°.

By a similar procedure, 5-*chlorobenzo*-1 : 3-*dioxole*-2-*carboxylic acid* (2·4 g.), from 4-chlorocatechol (14·45 g.), was isolated as colourless needles, m. p. 132—33° (from light petroleum) (Found: C, 48·0; H, 2·7%; equiv., 195. $C_8H_5O_4Cl$ requires C, 47·9; H, 2·5%; equiv., 200). Similarly 4 : 6-*dichlorobenzo*-1 : 3-*dioxole*-2-*carboxylic acid* (3·0 g.) was obtained from 3 : 5-dichlorocatechol (8·95 g.), as colourless needles, m. p. 149—149·5° (from light petroleum) (Found: C, 40·7; H, 1·7. $C_8H_4O_4Cl_2$ requires C, 40·9; H, 1·7%).

The unsubstituted acid (1·0 g.) in chlorobenzene (20 ml.) was treated with chlorine (0·45 g., 1 mole) at room temperature. After extraction from the mixture with sodium hydrogen carbonate solution, a crude dichloro-acid was isolated as a brown oily solid (0·9 g.). Repeated crystallisation gave the (? 5 : 6-)*dichlorobenzo*-1 : 3-*dioxole*-2-*carboxylic acid* as colourless needles, m. p. 145° (from ethyl acetate–light petroleum) (Found: C, 41·0; H, 1·8%). Mixed m. p. with the 4 : 6-dichloro-acid (*vide supra*) was 120—128°.

2 : 2-*Diisobutylbenzo*-1 : 3-*dioxole*.—Catechol (5·5 g.) and di*iso*butyl ketone (3·55 g.) were condensed in the presence of phosphoric oxide (7·5 g.), according to Slooff's method (*loc. cit.*). 2 : 2-*Diisobutylbenzo*-1 : 3-*dioxole* was isolated as a colourless oil (2·0 g.), b. p. 73—75°/0·5 mm., d_4^{18} 0·972 (Found : C, 76·6; H, 9·2. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%).

Attempted oxidation of this dioxole, or of the 2 : 2-dimethyl or 2-ethyl-2-methyl compound, with potassium permanganate in water or pyridine or with chromic oxide in acetic acid failed to yield dioxole-2-carboxylic acid.

Ethyl Bis-2 : 4-*dichlorophenoxyacetate*.—A solution of sodium 2 : 4-dichlorophenoxide, from the phenol (16·3 g.) and sodium (2·3 g.) in anhydrous ethanol, was added to ethyl dichloroacetate (31·4 g., 100% excess), and the mixture heated at reflux for 8 hr.; precipitation of sodium chloride was then complete. The mixture was worked up in the usual manner and the ethereal solution, after extraction of unchanged phenol, gave *ethyl bis*-2 : 4-*dichlorophenoxyacetate* (8·25 g.) finally isolated as slender colourless needles, m. p. 77°, from ethanol (Found : C, 47·0; H, 3·1. $C_{16}H_{12}O_4Cl_4$ requires C, 46·9; H, 3·0%). The ester was identified by hydrolysis to bis-2 : 4-dichlorophenoxyacetic acid, isolated as a potassium salt, m. p. 235° (decomp.), which on acidification gave the parent acid as colourless needles, m. p. 154° (Haskelberg, *J. Org. Chem.*, 1947, **12**, 426, records m. p. 152°). No half-condensation product, *i.e.*, ethyl α-chloro-2 : 4-dichlorophenoxyacetate, could be isolated from the original reaction.

meso-αα′-*Bis*-2 : 4-*dichlorophenoxysuccinic Acid*.—Methyl *meso*-dibromosuccinate (15·2 g.) was condensed with sodium 2 : 4-dichlorophenoxide, from dichlorophenol (16·3 g.), in the usual manner, meso-αα′-*bis*-2 : 4-*dichlorophenoxysuccinic acid* (8·5 g.) being obtained as colourless plates, m. p. 255° (decomp.; inserted in bath at 252° and losing water at the m. p.) (from aqueous ethanol) (Found : C, 43·5; H, 2·3. $C_{16}H_{10}O_6Cl_4$ requires C, 43·7; H, 2·3%).

Ethyl 2 : 4-*Dichlorophenyl Oxalate*.—Ethyl chloroglyoxylate (17 g.) in carbon tetrachloride (50 ml.) was stirred with 2 : 4-dichlorophenol (16·2 g.) in 2N-sodium hydroxide (75 ml.) containing some crushed ice. After 2 min. the carbon tetrachloride layer was separated, washed with ice-cold alkali, and dried ($MgSO_4$). After evaporation of the solvent, the *ester* distilled as a colourless oil (25 g.), b. p. 146—147°/2·5 mm. It crystallised as long colourless needles, m. p. 39°, from light petroleum (Found : C, 45·5; H, 3·0. $C_{10}H_8O_4Cl_2$ requires C, 45·7; H, 3·1%).

2 : 4-*Dichlorophenoxyacetone*.—Monobromoacetone (27·4 g.) was added to a hot solution of sodium 2 : 4-dichlorophenoxide [from the phenol (32·6 g.) and sodium (4·6 g.)] in ethanol (200 ml.); precipitation of sodium bromide was complete in 2 hr. The unchanged phenol was removed by alkaline extraction, and the product isolated as a colourless liquid (25 g.), b. p. 120—124°/1·5 mm., which rapidly solidified. Recrystallisation gave 2 : 4-*dichlorophenoxyacetone* as colourless prisms, m. p. 57°, from light petroleum (Found : C, 49·2; H, 3·65. $C_9H_8O_2Cl_2$ requires C, 49·3; H, 3·7%). The 2 : 4-*dinitrophenylhydrazone* formed orange prisms, m. p. 155°, from alcohol (Found : C, 45·0; H, 2·9; N, 14·2. $C_{15}H_{12}O_5N_4Cl_2$ requires C, 45·1; H, 3·0; N, 14·0%).

Dr. E. Challen is thanked for microanalyses.

School of Applied Chemistry, N.S.W. University of Technology,
Sydney, Australia. [*Received, December 28th*, 1953.]

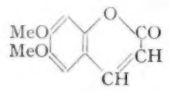
The Chemistry of Extractives from Hardwoods. Part XVI. Coumarin Constituents of* Fagara macrophylla, Zanthoxylum flavum, *and* Chloroxylon swietenia.

By F. E. King, J. R. Housley, and T. J. King.

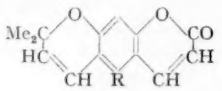
[Reprint Order No. 4932.]

The principal crystalline heartwood extractives of *Fagara macrophylla* (olon), of *Zanthoxylum flavum* (alternatively *Fagara flava*) (West Indian satinwood), and of a third species *Chloroxylon swietenia* (East Indian satinwood) also believed to be of the same family, Rutaceae, are coumarins, some of them already known as products of other *Zanthoxylum* species. 6 : 7-Dimethoxycoumarin (æsculetin dimethyl ether) and 6 : 7 : 8-trimethoxycoumarin are present in olon; suberosin (7-methoxy-6-*iso*pent-2′-enylcoumarin) and psoralene [furano(2′ : 3′-6 : 7)coumarin] have been found in W. Indian satinwood; and E. Indian satinwood contains xanthyletin [2′ : 2′-dimethylpyrano(5′ : 6′-6 : 7)coumarin], xanthoxyletin (5-methoxyxanthyletin), and the related but previously unknown phenol, 7-demethylsuberosin.

The genus *Zanthoxylum* (family Rutaceae) with the sub-genus *Fagara* (regarded as synonymous in the Bentham and Hooker classification) consist approximately of 150—200 species of shrubs and trees, including a few well-known as a source of furniture woods. Chemical investigations on some 30 species have been reported in the literature but they chiefly concern constituents of the bark, roots, leaves, or fruit. The principal compounds so far isolated are alkaloids, *e.g.*, skimmianine and berberine, and coumarin derivatives. Among the latter are 6 : 7-dimethoxycoumarin (æsculetin dimethyl ether) (I) found in the leaves of *Z. setosum* (Araki and Miyashita, *J. Pharm. Soc. Japan*, 1928, **48**, 437), and those present in the bark of *Z. americanum*, namely, xanthyletin (II; R = H), xanthoxyletin (II; R = OMe), and *allo*xanthoxyletin, of which the structures were determined by



(I)



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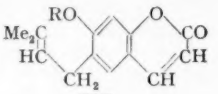


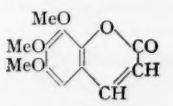
(III)

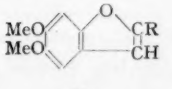
Robertson and his collaborators (Bell, Robertson, and Subramaniam, *J.*, 1936, 627; Bell and Robertson, *J.*, 1936, 1828; Robertson and Subramaniam, *J.*, 1937, 286; Bell, Bridge, and Robertson, *J.*, 1937, 1542). Closely related to xanthyletin is the 7-methoxy-6-*iso*pent-2′-enylcoumarin, suberosin (III; R = Me), recently isolated from the bark of *Z. suberosum* (Ewing, Hughes, and Ritchie, *Austral. J. Sci. Res.*, 1950, **3**, *A*, 342).

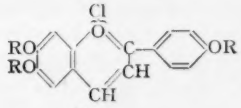
Previous investigations on woods of *Zanthoxylum* species appear to have been limited to West Indian satinwood (*Z. flavum*) from which were isolated two unidentified lactones, $C_{11}H_{10}O_3$, m. p. 124—126°, and $C_{14}H_{12}O_3$, m. p. 133° (Auld and Pickles, *J.*, 1912, **101**, 1052). Once readily available, *e.g.*, from Cuba, Jamaica, Puerto Rico, this valuable decorative wood has been almost entirely eliminated from these W. Indian islands (personal communication from Mr. F. H. Wadsworth, Forestry Service, U.S. Department of Agriculture), but sufficient was ultimately procured to enable a re-examination of the heartwood extractives to be undertaken. The extractable constituents of the somewhat similar W. African timber olon (*Fagara macrophylla*) and of East Indian satinwood (*Chloroxylon swietenia*) have also been studied since it was of interest to ascertain the existence of any chemical relation between these species in view of uncertainties about the classification of *C. swietenia* with respect to the families Rutaceae and Meliaceae (cf. Metcalfe and Chalk, "Anatomy of the Dicotyledons," Clarendon Press, Oxford, 1950, pp. 356, 357). All three timbers are said to be resistant to decay and to the attack of termites (personal communication from Mr. B. J. Rendle, D.S.I.R. Forest Products Research Laboratory).

* Part XV, *J.*, 1953, 4158.

Extraction of coarsely powdered olon with boiling light petroleum yielded a mixture of a crystalline solid and an involatile oil. A further quantity of the solid was obtained from the subsequent ether-extraction and it was resolved by crystallisation into 6 : 7-dimethoxycoumarin (I) and 6 : 7 : 8-trimethoxycoumarin (IV), the latter not formerly known as a natural product. The coumarin (I) was also isolated from the succeeding acetone extract, and the total yield amounted to 2·3% of the wood. The average content of the


(IV)

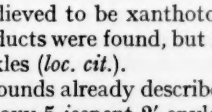

(V)

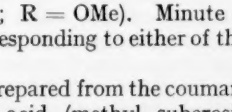

(VI)

trimethoxycoumarin (IV) was 0·18%; it has m. p. 104° and may be identical with the unidentified substance, m. p. 104°, obtained together with (I) from *Z. setosum* by Araki and Miyashita (*loc. cit.*). A compound $C_{15}H_{13}O_2{\cdot}OMe$ and an alkaloid $C_{20}H_{21}O_7N$, isolated as hydrochloride, were also found in the extracts but were present in amounts too small for detailed investigation.

The structure of the major constituent (I) was confirmed by its conversion with methyl sulphate and alkali into 2 : 4 : 5-trimethoxycinnamic acid and by its formation of 2-acetoxy-4 : 5-dimethoxycinnamic acid. Similarly, the trimethoxycoumarin (IV) yielded 2 : 3 : 4 : 5-tetramethoxycinnamic acid, oxidised to 2 : 3 : 4 : 5-tetramethoxybenzoic acid (Wessely and Demmer, *Ber.*, **1928**, **61**, 1279). Bromination of 6 : 7-dimethoxycoumarin led invariably to the 3-bromo-derivative and not to the dibromocoumarin described by Araki and Miyashita (*loc. cit.*). The action of aqueous hot alkali on the 3-bromo-compound gave 5 : 6-dimethoxycoumarone-2-carboxylic acid (V; R = CO_2H), which was decarboxylated in quinoline to 5 : 6-dimethoxycoumarone (V; R = H) (Tanaka, *J. Amer. Chem. Soc.*, 1951, **73**, 872). From the coumarin (I) and *p*-methoxyphenylmagnesium bromide 6 : 7 : 4′-trimethoxyflavylium chloride (VI; R = Me) was prepared and hence the salt (VI; R = H).

The principal crystalline component of the viscous oil dissolved by boiling petroleum from W. Indian satinwood was suberosin (III; R = Me); it crystallised from methanol, and from the remaining solution a small amount of psoralene (VII; R = H) was obtained. Further limited quantities of both compounds were derived from the succeeding extraction with ether [total yields, of (III; R = Me) 0·85%, of (VII; R = H) 0·055%], and traces

(VII) 

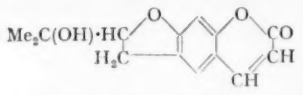
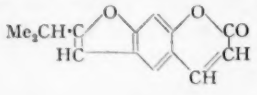
 (VIII)

of a coumarin believed to be xanthotoxin (VII; R = OMe). Minute quantities of other unrecognised products were found, but none corresponding to either of the lactones reported by Auld and Pickles (*loc. cit.*).

Various compounds already described were prepared from the coumarin (III; R = Me), *e.g.*, 2 : 4-dimethoxy-5-*iso*pent-2′-enylcinnamic acid (methyl suberosinic acid; Ewing *et al.*, *loc. cit.*); it was oxidised to acetone and 7-methoxycoumarin-6-aldehyde (Ewing, *et al.*, *loc. cit.*) and was cyclised to dihydroxanthyletin when heated with hydrobromic acid. A tribromo-derivative, believed to be 3 : 2′ : 3′-tribromosuberosin, and an epoxide were prepared; in view of the failure of coumarin to react with monoperphthalic acid (Dean, *Fortschritte der Chemie Organischer Naturstoffe*, 1952, **9**, 231), the epoxide is regarded as the 2′ : 3′-compound. With boiling oxalic acid, the oxide was hydrated to a crystalline diol; with boiling dilute sulphuric acid it isomerised to the 2′-keto-compound (VIII). The 2′ : 2′-dimethylchromen synthesised from suberosin and excess of methylmagnesium iodide was an oil.

The light petroleum and ether extracts of E. Indian satinwood consisted of viscous liquids from which appreciable quantities of crystalline compounds were isolated, *i.e.*, xanthyletin (II; R = H) (3·3%), xanthoxyletin (II; R = OMe) (0·1%), and a phenolic coumarin $C_{14}H_{14}O_3$ (1·3%). Further small amounts of (II; R = H) and of the phenolic

constituent from the later acetone treatment of the wood have been included in the percentage yields. Xanthyletin and xanthoxyletin were identified by mixed m. p. with specimens kindly provided by Professor A. Robertson, F.R.S., and by the preparation of the dihydro-derivatives. Dihydroxanthyletin gave a 3-bromo-derivative converted

(IX)   (X)

by alkalis into 2′ : 2′-dimethyldihydropyrano(5′ : 6′-5 : 6)benzofuran-2-carboxylic acid, which was decarboxylated to the corresponding dihydrodimethylpyranobenzofuran.

The new phenolic coumarin gave suberosin (III; R = Me) when methylated with diazomethane, and dihydroxanthyletin under catalysis with hot dilute hydrochloric acid, and it was thereby recognised as 7-demethylsuberosin (III; R = H). Through the action of monoperphthalic acid demethylsuberosin undergoes oxidation at the 2′-position and cyclisation to a compound (IX) which is therefore the racemic form of the natural products (−)-nodakenetin and (+)-marmesin (Chatterjee and Mitra, *J. Amer. Chem. Soc.*, 1949, **71**, 606). As with marmesin, the structure (IX) is confirmed by dehydration with phosphoric oxide to deoxyoreosolone (X).

Experimental

Light absorption data refer to solutions in ethanol.

Extraction of Olon (Fagara macrophylla).—The coarsely ground wood (3·5 kg.) was extracted for 18 hr. with boiling light petroleum (b. p. 60—80°). Crystalline solid was collected from the cold solution, and a further crop was obtained by triturating with ether (50 c.c.) the syrupy residue obtained by evaporation of the petroleum filtrate. Crystallisation of the combined solids from methanol gave first 6 : 7-dimethoxycoumarin (I) (23—24 g.) and then 6 : 7 : 8-trimethoxycoumarin (IV) (5·3 g.). The material left in the ether was a pale orange oil (11 g.) neutral and unsaponifiable, and resolved by chromatography on alumina into several fractions of which one (eluted with benzene) crystallised from benzene–light petroleum in *needles* (0·2 g.), m. p. 122—123° (Found: C, 75·2; H, 6·6; OMe, 12·6. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3; OMe, 12·1%); light absorption: max., 226 mμ; log ε 3·95.

Subsequent treatment of the wood with boiling ether extracted a gummy solid from which the coumarins (I) (6·6 g.) and (IV) (1 g.) were isolated by crystallisation from methanol. Chromatographic fractionation of the residue (3 g.) yielded a further amount (0·1 g.) of the substance, m. p. 122—123°.

From the petroleum- and ether-extracted wood boiling acetone removed a resin (*ca.* 100 g.) which when triturated with cold methanol gave a further quantity (51 g.) of the coumarin (I) (total yield 81 g., 2·3%). Finally, extraction with boiling ethanol afforded a brittle dark brown resin (30 g.) from which no homogeneous substance was obtained.

The residue from the acetone-soluble portion of the wood was in one case extracted with boiling water (3 × 350 c.c.). Concentration of the aqueous solution to 500 c.c. and treatment with concentrated hydrochloric acid (10 c.c.) precipitated a yellow crystalline *hydrochloride* (0·2 g.) which crystallised from methanol in needles, m. p. 276° (decomp.) (Found: C, 56·5; H, 5·4; N, 3·3; Cl, 8·7; OMe, 9·0; NMe, 9·74. $C_{20}H_{21}O_7N$,HCl requires C, 56·7; H, 5·2; N, 3·3; Cl, 8·4; 1OMe, 7·3; 1NMe, 6·8%). The amorphous base gave precipitates with the usual alkaloid reagents and with gallic acid in concentrated sulphuric acid a turquoise blue colour indicative of a methylenedioxy-group.

6 : 7-*Dimethoxycoumarin* (I).—The coumarin (I) crystallised in colourless needles, m. p. 143—143·5°, its alcoholic solution exhibiting a strong blue-violet fluorescence (Found: C, 63·7; H, 4·8; OMe, 30·8. Calc. for $C_{11}H_{10}O_4$: C, 64·1; H, 4·9; 2OMe, 30·0%); light absorption: max., 229, 294 and 342 mμ; log ε 4·23, 3·76, 4·1. With boiling aqueous potassium hydroxide the coumarin gave *trans*-2-hydroxy-4 : 5-dimethoxycinnamic acid, yellow prisms (from methanol), m. p. 197—198° (Araki and Miyashita, *loc. cit.*, give m. p. 197—198°); this gave an acetate, needles (from methanol), m. p. 210—211° (*idem*, *loc. cit.*, give m. p. 210—211°) (Found: C, 58·2; H, 5·2; OMe, 25·3. Calc. for $C_{13}H_{14}O_6$: C, 58·6; H, 5·3; 2OMe, 23·3%), and methyl ether, yellow prisms (from ethanol), m. p. 168° (*idem*, *ibid.*, 1929, **49**, 736, give m. p. 168°) (Found: C, 60·3; H, 5·7; OMe, 41·3. Calc. for $C_{12}H_{14}O_5$: C, 60·5; H, 5·9;

3OMe, 39·1%). Bromination of the coumarin in cold acetic acid, benzene, or chloroform gave the monobromo-derivative, needles (from ethanol), m. p. 178—179° (*idem, ibid.*, 1928, **48**, 437, give m. p. 176°) (Found: C, 46·1; H, 2·9; Br, 26·1. Calc. for $C_{11}H_9O_4Br$: C, 46·3; H, 3·2; Br, 28·0%); light absorption: max., 234, 258, 306, 356 mμ; log ε 4·17, 3·83, 3·83, 4·2. Demethylation of the coumarin with boiling hydrobromic acid in acetic acid gave æsculetin, prisms (from ethanol), m. p. 268—269° (Glaser and Kraus, *Biochem. Z.*, 1923, **138**, 183, give m. p. 270°) (Found: C, 60·6; H, 3·8. Calc. for $C_9H_6O_4$: C, 60·7; H, 3·4%).

5 : 6-*Dimethoxycoumarone-2-carboxylic Acid* (V; R = CO_2H).—3-Bromo-6 : 7-dimethoxycoumarin (3·0 g.) was treated with aqueous potassium hydroxide (10%; 150 c.c.) at the b. p. for 1 hr. and the resulting orange solution poured into excess of hydrochloric acid (5N). The precipitated 5 : 6-dimethoxycoumarone-2-carboxylic acid (2·25 g., 97%) after two precipitations from a solution in sodium hydrogen carbonate separated from ethanol in colourless needles, m. p. 242—244° (decomp.) (Found: C, 59·1; H, 4·5; OMe, 28·3. Calc. for $C_{11}H_{10}O_5$: C, 59·5; H, 4·5; 2OMe, 27·9%). [Tanaka, *loc. cit.*, gives m. p. 245° (decomp.)]. Esterification with methanol–hydrogen chloride gave the *methyl ester*, needles (from methanol), m. p. 140—142° (Found: C, 60·7; H, 5·0; OMe, 38·1. $C_{12}H_{12}O_5$ requires C, 61·0; H, 5·1; 3OMe, 39·4%).

5 : 6-*Dimethoxycoumarone* (V; R = H).—The above acid (V; R = CO_2H) (1·9 g.) was heated at 220° in quinoline (10 c.c.) with copper powder (0·4 g.) until the evolution of carbon dioxide ceased (30 min.). The cooled mixture was poured into ether and filtered and, after the quinoline had been removed by dilute hydrochloric acid, the ethereal layer was washed with water, dried, and evaporated. The residue was a straw-yellow oil which, purified by passage down an alumina column in light petroleum (b. p. 40—60°) solution, crystallised from light petroleum (b. p. 40—60°) giving the coumarone (V; R = H) as colourless needles (0·9 g., 60%), m. p. 54—55° (Found: C, 67·3; H, 5·8; OMe, 32·8. Calc. for $C_{10}H_{10}O_3$: C, 67·4; H, 5·7; 2OMe, 34·8%) (Tanaka *loc. cit.*, gives m. p. 53—54°).

6 : 7 : 4′-*Trimethoxyflavylium Chloride* (VI; R = Me).—6 : 7-Dimethoxycoumarin (2·5 g.) in dry benzene (250 c.c.) was slowly added to a stirred solution of *p*-methoxyphenylmagnesium bromide prepared from excess of *p*-bromoanisole (7·5 g.) in ether (20 c.c.). After 1 hr. the mixture was treated with concentrated hydrochloric acid (6 c.c.), and the dark green deposit collected and washed successively with benzene, ether, and dilute hydrochloric acid. The dried residue (3·8 g., 95%) was crystallised from 1% aqueous hydrochloric acid, giving the *flavylium chloride* (VI; R = Me) as a brown mass of microscopic orange needles with a green lustre, m. p. 158° (decomp.) (Found: C, 58·8; H, 6·1. $C_{18}H_{17}O_4Cl,2H_2O$ requires C, 58·6; H, 5·7. Found, after drying at 100° in a vacuum: C, 65·4; H, 5·9; loss, 9·2. $C_{18}H_{17}O_4Cl$ requires C, 65·0; H, 5·1; loss, 9·8%). Solutions of the flavylium salt in dilute aqueous acid have a very intense green fluorescence.

Demethylation of the compound with hydriodic acid followed by conversion of the product into the chloride (cf. Willstätter, Zechmeister, and Kindler, *Ber.*, 1924, **57**, 1938) gave 6 : 7 : 4′-*trihydroxyflavylium chloride* (VI; R = H) (64%) as vermilion microscopic plates (from methanolic hydrochloric acid), m. p. 290° (decomp.), sinters at 250° (Found: C, 60·3; H, 4·3. $C_{15}H_{11}O_4Cl,\frac{1}{2}H_2O$ requires C, 60·1; H, 4·0%) (Hoyashi, *Acta Phytochim.*, Tokyo, 1935, **8**, 179, gives m. p. 284, sinters at 250°, but apparently no analysis). Solutions of the salt in mineral acid are orange-red, becoming carmine-red on the addition of alkali and then fading, after 24 hr., to yellow. With sodium acetate, solutions of the flavylium salt give a bright red precipitate. The ferric reaction of the salt in ethanol is red-brown.

6 : 7 : 8-*Trimethoxycoumarin* (IV).—The coumarin (total yield, 0·18%) crystallised from methanol or benzene–light petroleum in large thick colourless prisms, m. p. 104° (Wessely and Demmer, *loc. cit.* give m. p. 104°) [Found: C, 60·7; H, 5·1; OMe, 40·5%; *M* (Rast), 232. Calc. for $C_{12}H_{12}O_5$: C, 61·0; H, 5·1; 3OMe, 39·4%; *M*, 236].

2 : 3 : 4 : 5-*Tetramethoxycinnamic Acid*.—Alkaline hydrolysis of the trimethoxycoumarin (IV) and methylation with methyl sulphate by the method of Wessely and Demmer (*loc. cit.*) gave 2 : 3 : 4 : 5-*tetramethoxycinnamic acid* not isolated by these authors, which crystallised in needles from aqueous ethanol, m. p. 81—82° (Found: C, 58·3; H, 6·4; OMe, 45·9. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0; 4OMe, 46·2%). Oxidation of this acid with alkaline permanganate gave 2 : 3 : 4 : 5-tetramethoxybenzoic acid, m. p. 85—85·5° (*idem, loc. cit.*, give m. p. 85°) (Found: C, 54·7; H, 5·7; OMe, 50·1. Calc. for $C_{11}H_{14}O_6$: C, 54·5; H, 5·8; 4OMe, 51·2%).

Extraction of West Indian Satinwood (Zanthoxylum flavum).—Extraction of the ground wood (4 kg.) with boiling light petroleum for 18 hr. and evaporation gave a viscous orange oil (140 g.) having a strong coconut odour. After several hours at 0° the oil was decanted from the portion which had solidified, and the solid separated by crystallisation from methanol into

suberosin (III; R = Me) (29 g.) and the more-soluble psoralene (VII; R = H) (0·8 g.). The residual oil contained no detectable amount of steam-volatile material and only traces of alkali-soluble products, *e.g.*, suberosin (0·7 g.), which was extracted with 8% aqueous sodium hydroxide. In chromatography on alumina, 97% was eluted with light petroleum. After refluxing with excess of 1% methanolic potassium hydroxide and removal of the gummy acid fraction (2 g.), the neutral oil (64 g.) gave suberosin (1 g.) and a crystalline alcohol (0·3 g.), needles (from light petroleum), m. p. 107—109°, $[\alpha]_D^{20}$ +56° in $CHCl_3$ (Liebermann–Burchard reaction, red, fluorescing green) (Found, after drying at 120°: C, 84·2; H, 11·8. $C_{30}H_{50}O$ requires C, 84·6; H, 11·8%). Finally, distillation of the oil (27 g.) gave two fractions (*a*) b. p. (from sodium) 140—150°/0·05 mm. (1·3 g.) (Found: C, 75·7; H, 10·8%) and (*b*) b. p. 158—172°/0·05 mm. (0·25 g.) consisting of suberosin.

Further extraction of the wood with ether and evaporation of the solution gave a viscous red oil (40 g.) which, after 3 days at 0°, deposited a solid separated by crystallisation from methanol into suberosin (0·8 g.), psoralene (1·4 g.), and a third coumarin (0·026 g.) regarded as xanthotoxin and separating from light petroleum as needles, m. p. 144—145° [Found: C, 66·5; H, 3·9; OMe, 14·1%; *M* (Rast), 213. Calc. for $C_{12}H_8O_4$: C, 66·7; H, 3·7; 1OMe, 14·3%; *M*, 216]. Xanthotoxin has m. p. 145—146° (Thoms, *Ber.*, 1911, **44**, 3325). Treatment of the non-crystalline part of the extract by alkali-extraction, chromatography, hydrolysis, and distillation failed to yield any further pure material. The acetone extract mainly consisted of a dark phenolic resin (160 g.) from the neutral part of which suberosin (3·1 g.) was obtained by crystallisation from a small volume of acetone. Extraction of the wood with ethanol gave only resinous material (20 g.).

Suberosin (*7-Methoxy-6-isopent-2′-enylcoumarin*) (III; R = Me).—Suberosin (total yield 34·1 g., 0·85%) crystallised in large rhombic prisms, m. p. 87—88°, from methanol (Ewing *et al.*, *loc. cit.*, give m. p. 87·5°) [Found: C, 73·5; H, 6·9; OMe, 14·5%; *M* (Rast), 231. Calc. for $C_{15}H_{16}O_3$: C, 73·7; H, 6·6; 1OMe, 12·7%; *M*, 244]; light absorption: max. 224, 253, 332 mμ; log ε, 4·34, 3·76, 4·18. Hot aqueous sodium hydroxide and methyl sulphate gave methylsuberosinic acid, yellow prisms, m. p. 134—135°, from aqueous ethanol (*idem*, *loc. cit.*, give m. p. 134—135°) (Found: C, 69·4; H, 7·3; OMe, 21·3. Calc. for $C_{16}H_{20}O_4$: C, 69·5; H, 7·3; 2OMe, 22·5%) which gave an oily methyl ester. The oxidation of suberosin with chromic acid in acetic acid at room temperature gave acetone, identified as the 2 : 4-dinitrophenylhydrazone, and 7-methoxycoumarin-6-aldehyde, m. p. 252—253° (*idem*, *loc. cit.*, give m. p. 252—253°) (Found: C, 63·9; H, 4·1; OMe, 13·9. Calc. for $C_{11}H_8O_4$: C, 64·7; H, 4·0; OMe, 15·2%). The dibromide prepared by bromination at room temperature in benzene crystallised from ethanol as plates, m. p. 148° (*idem*, *loc. cit.*, give m. p. 148°) (Found: C, 44·6; H, 4·3; Br, 40·1. Calc. for $C_{15}H_{16}O_3Br_2$: C, 44·6; H, 4·0; Br, 39·6%); light absorption: max., 222, 326 mμ; log ε, 3·93, 3·75.

Dihydroxanthyletin.—Suberosin (2 g.) was refluxed for 1 hr. with aqueous hydrobromic acid (150 c.c.; *d* 1·49) containing red phosphorus (1 g.), and the resulting solution poured on ice and extracted with ether. The alkali-insoluble portion of the ethereal extract crystallised from light petroleum (b. p. 60—80°) in elongated plates (0·2 g.), m. p. 122—124° alone and mixed with an authentic specimen of dihydroxanthyletin (Found: C, 72·9; H, 6·2. Calc. for $C_{14}H_{14}O_3$: C, 73·0; H, 6·1%).

Tribromosuberosin.—Suberosin (1 g.) in glacial acetic acid (5 c.c.) was treated with a solution of bromine (1·32 g., 2 mols.) in acetic acid (10 c.c.). After 1 hr. the solvent was removed under reduced pressure, the residue of *tribromosuberosin* crystallising from ethanol in colourless prisms, m. p. 170° (Found: C, 37·6; H, 3·5; Br, 49·5. $C_{15}H_{15}O_3Br_3$ requires C, 37·3; H, 3·1; Br, 49·7%); light absorption: max., 226, 340 mμ; log ε 4·24, 4·26. Solutions of the compound show a blue-violet fluorescence.

Complex of Suberosin and 2 : 4-Dinitrophenylhydrazine Sulphate.—Suberosin dissolved in the minimum amount of methanol and treated with an excess of saturated methanolic 2 : 4-dinitrophenylhydrazine sulphate gave a *complex* (95%), m. p. 167—168°, crystallising from ethanol or acetic acid in yellow plates (Found: C, 46·1; H, 4·5; N, 10·2; S, 5·2. $C_{15}H_{16}O_3,C_6H_6O_4N_4,H_2SO_4$ requires C, 46·5; H, 4·5; N, 10·4; S, 5·9%). The complex was resolved into its components on an alumina column, light petroleum eluting the coumarin and benzene the remaining hydrazine sulphate. The light absorptions of the complex and of equimolecular solutions of the coumarin and the hydrazine sulphate in separate cells placed in series in the spectrophotometer were indistinguishable.

Suberosin 2′ : 3′-Epoxide.—Suberosin (2 g.) in dry ether (75 c.c.) was treated with a solution of monoperphthalic acid (1·6 g.) in dry ether (25 c.c.) at 0° for 24 hr. After being washed with

aqueous sodium hydrogen carbonate, the ethereal solution was dried and evaporated, the residue (1·8 g.) of *epoxide* crystallising from benzene in prisms, m. p. 114—114·5° (Found: C, 68·7; H, 6·1; OMe, 12·0. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2; OMe, 11·9%). The compound gave an orange-coloured solution with a violet fluorescence in concentrated sulphuric acid.

Dihydro-2′ : 3′-dihydroxysuberosin.—Suberosin epoxide (0·52 g.) was treated with boiling aqueous oxalic acid (1%) for 1 hr. (cf. Böhme and Pietsch, *Ber.*, 1939, **72**, 773) and the resulting *diol* crystallised from chloroform–light petroleum as small cubic prisms, m. p. 136—137° (Found: C, 64·6; H, 6·4. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%). Rapid precipitation after boiling in chloroform solution for 5 min. gave elongated yellow prisms, m. p. 129—131°, which reverted to the colourless form after several days at room temperature. The compound in concentrated sulphuric acid gave a bright red solution with a violet fluorescence.

Dihydro-2′-oxosuberosin (VIII).—Suberosin epoxide (0·8 g.) was heated with dilute sulphuric acid (20%) for 4 hr. (cf. *idem, loc. cit.*); the product then crystallised from chloroform–light petroleum as colourless plates, m. p. 92—93°, consisting of *dihydro-2′-oxosuberosin* (0·7 g.) (Found: C, 69·5; H, 6·3. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%). The *oxime* formed colourless needles, m. p. 169—170°, from aqueous ethanol (Found: C, 65·7; H, 6·1; N, 4·7. $C_{15}H_{17}O_4N$ requires C, 65·4; H, 6·2; N, 5·1%).

7-Methoxy-2 : 2-dimethyl-6-isopent-2′-enylbenzopyran.—Suberosin (2 g.) in ether (200 c.c.) was added slowly to a solution of excess of methylmagnesium iodide (from 6·5 g. of methyl iodide) in ether (100 c.c.). The solution was boiled for 3 hr. and then treated with dilute hydrochloric acid. The product was isolated with ether in the usual way, distillation affording the *benzopyran* as an oil (1 g.), b. p. 90—92°/0·05 mm., n_D^{20} 1·5493 (Found: C, 78·7; H, 8·3; OMe, 10·5. $C_{17}H_{22}O_2$ requires C, 79·0; H, 8·6; OMe, 12·0%).

Psoralene (VII; R = H).—Crystallised from benzene–light petroleum or methanol psoralene formed large colourless needles, m. p. 161—162° (Jois, Manjunath, and Rao, *J. Indian Chem. Soc.*, 1933, **10**, 41, give m. p. 161—162°) [Found: C, 70·5; H, 3·3%; *M* (Rast), 189. Calc. for $C_{11}H_6O_3$: C, 71·0; H, 3·3%; *M*, 186]. Treatment with potassium hydroxide–methyl sulphate in the usual way converted psoralene into β-(6-methoxy-5-coumaronyl)acrylic acid which separated as pale yellow needles, m. p. 163—165°, from benzene–light petroleum or aqueous ethanol (Jois and Manjunath, *Ber.*, 1937, **70**, 434, give m. p. 163—165°) (Found: C, 66·2; H, 4·5; OMe, 14·2. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6; 1OMe, 14·1%).

Extraction of East Indian Satinwood (Chloroxylon swietenia).—The coarsely ground wood (3·6 kg.) was extracted for 120 hr. with boiling light petroleum (b. p. 40—60°). The cooled solution was decanted from the semi-crystalline deposit which gave xanthyletin (79·6 g.) by crystallisation from methanol. The contents of the residual methanolic solution and of the light petroleum solution were separated by 8% aqueous sodium hydroxide into phenolic (65 g.) and neutral (35 g.) fractions. The neutral fraction when crystallised from methanol gave xanthyletin (8·4 g.) and the xanthyletin–xanthoxyletin complex (8·5 g.), m. p. 99—104°, previously described by Robertson and Subramaniam (*J.*, 1937, 1549). Treatment of the mother-liquors from this fraction with 60% aqueous alkali at 100° (10 min.) followed by dilution and extraction with ether left an aqueous solution from which carbon dioxide precipitated a solid separated by methanol into xanthoxyletin (3·85 g.) and a further amount (8·5 g.) of the above complex.

Crystallisation of the phenolic fraction from benzene gave *7-demethylsuberosin* (24·0 g.), a further quantity being isolated from the mother-liquor as the acetate (26 g.).

The following ether-extract, an orange oil (98 g.), was also separated into phenolic and non-phenolic fractions. The neutral fraction treated as above with alkali gave xanthyletin (15 g.) and the xanthyletin–xanthoxyletin complex (11 g.). The phenolic portion of the extract when crystallised gave 7-demethylsuberosin (16 g.), a further quantity being isolated as acetate (23 g.).

Further extraction of the wood with acetone gave a resinous mass (143 g.) of which some 50% was ether-soluble, and was separated into phenolic and non-phenolic fractions. The former gave 7-demethylsuberosin (8·1 g.) when crystallised from benzene, and from a methanol solution of the neutral portion xanthyletin (16·7 g.) was obtained.

Xanthyletin (II; R = H).—Xanthyletin (total yield 120 g., 3.3% approx.) crystallised from methanol in elongated flat prisms, m. p. and mixed m. p. 126—127° [Found: C, 73·4; H, 5·5%; *M* (Rast), 235. Calc. for $C_{14}H_{12}O_3$: C, 73·7; H, 5·3%; *M*, 228]; light absorption: max., 266, 348 mμ; log ε 4·34, 4·15. The dihydro-derivative prepared by reduction in ethanol with palladium at normal temperature and pressure formed elongated plates, m. p. 122—124°, from benzene–light petroleum (Bell and Robertson, *loc. cit.*, give m. p. 124—125°) (Found: C, 72·9; H, 6·2. Calc. for $C_{14}H_{14}O_3$: C, 73·0; H, 6·1%). Hot alkali and methyl sulphate

converted xanthyletin into *O*-methylxanthyletenic acid, yellow prisms (from methanol), m. p. 191—192° (decomp.) [*idem, loc. cit.*, give m. p. 193—194° (decomp.)] (Found: C, 69·4; H, 6·3; OMe, 12·7. Calc. for $C_{15}H_{16}O_4$: C, 69·2; H, 6·2; OMe, 11·9%). Alkaline hydrolysis of xanthyletin, in addition to acetone and resorcinol (Bell and Robertson, *loc. cit.*), gave acetaldehyde. The aqueous distillate from the hydrolysis mixture was treated with aqueous dimedone, acetaldehyde–dimedone complex being collected after 24 hr. and identified by comparison with an authentic specimen. Acetone isolated by distillation from the mother-liquors was identified as 2 : 4-dinitrophenylhydrazone.

Xanthoxyletin (II; R = OMe).—Xanthoxyletin (total yield 0·1% approx.) crystallised from methanol in colourless elongated prisms, m. p. and mixed m. p. 132—133° [Found: C, 69·5; H, 5·6; OMe, 12·2%; *M* (Rast), 259. Calc. for $C_{15}H_{14}O_4$: C, 69·7; H, 5·5; OMe, 12·0%; *M*, 258]. Dihydroxanthoxyletin, obtained by reduction with palladium and hydrogen, had m. p. 143—144° (*idem, loc. cit.*, give m. p. 144·5—145·5°) (Found: C, 69·3; H, 6·5; OMe, 11·9. Calc. for $C_{15}H_{16}O_4$: C, 69·2; H, 6·2; 1OMe, 11·9%).

3-*Bromodihydroxanthyletin.*—Dihydroxanthyletin (12 g.) in glacial acetic acid (200 c.c.) was treated with bromine (8·5 g., 1 mol.) in acetic acid (30 c.c.). After 2 hr. the solvent was removed under reduced pressure and the residue of 3-*bromodihydroxanthyletin* (16 g.) crystallised from benzene as flat elongated prisms, m. p. 163—164° (Found: C, 54·5; H, 4·5; Br, 25·8. $C_{14}H_{13}O_3Br$ requires C, 54·4; H, 4·2; Br, 25·8%).

Dihydro-2′ : 2′-dimethylpyrano(5′ : 6′-5 : 6)coumarone-2-carboxylic Acid.—3-Bromodihydroxanthyletin (15 g.) in aqueous potassium hydroxide (250 c.c., 10%) was heated under reflux for 1 hr. The cooled solution was poured into excess of hydrochloric acid, and the precipitate was collected and crystallised from methanol, the *acid* separating as glistening plates (6·5 g.), m. p. 242—244° (decomp.) (Found: C, 68·5; H, 5·3. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). The *methyl ester* prepared in methanol–hydrogen chloride crystallised from light petroleum as elongated flat prisms, m. p. 105—106° (Found: C, 69·0; H, 6·1. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%).

Dihydro-2′ : 2′-dimethylpyrano(5′ : 6′-5 : 6)coumarone.—The coumarone-carboxylic acid (6·2 g.) was heated in boiling quinoline (20 c.c.) containing copper powder (0·5 g.) for 12 min. The cooled solution was poured into ether, and the quinoline removed from the filtered solution by dilute hydrochloric acid. The ethereal solution was dried, and decolourised by passing it through alumina. Distillation gave a fraction (2·6 g., 51%), b. p. 153—155°/13 mm., which crystallised from a small volume of light petroleum (b. p. 40—60°) at 0°, the *coumarone* separating in large prisms, m. p. 39—41° (Found: C, 77·2; H, 6·8. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%). Its solution in concentrated sulphuric acid was orange changing to brown, red, purple, and finally blue. The *picrate* prepared in methanol, separated in bright red needles, m. p. 88—89° (Found: C, 53·1; H, 3·7; N, 9·7. $C_{13}H_{14}O_2,C_6H_3O_7N_3$ requires, C, 52·9; H, 4·0; N, 9·7%).

7-*Demethylsuberosin* (III; R = H).—7-Demethylsuberosin (yield 1·3%) crystallised from benzene in flat elongated prisms, m. p. 133·5—134° [Found: C, 73·3; H, 6·3%; *M* (Rast), 227. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%; *M*, 230]; light absorption: max., 226, 334 mμ; log ε 4·12, 4·21. The compound is readily soluble in dilute alkali to a yellow solution with a blue fluorescence; in sulphuric acid it gives a pale straw-yellow colour with a blue-violet fluorescence. It is very soluble in methanol and acetone, moderately soluble in benzene, chloroform, and ethyl acetate, and very sparingly soluble in light petroleum. Methylation at 0° for 18 hr. in ether with an excess of diazomethane gave suberosin, m. p. and mixed m. p. 87—88° (Found: C, 74·3; H, 6·8; OMe, 13·7. Calc. for $C_{15}H_{16}O_3$: C, 73·8; H, 6·6; 1OMe, 12·7%). When 7-demethylsuberosin was boiled in aqueous-alcoholic hydrochloric acid (0·2N) for 3 hr. and the solution diluted, dihydroxanthyletin was obtained (yield, 90%), m. p. and mixed m. p. 122—124° (Found: C, 73·5; H, 6·3. Calc. for $C_{14}H_{14}O_3$: C, 73·0; H, 6·1%). The *acetate* (acetic anhydride–pyridine) separated from aqueous ethanol in elongated prisms or from benzene in shining plates, m. p. 98—100° (Found: C, 70·9; H, 5·6; $CH_3{\cdot}CO$, 16·6. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9; $1CH_3{\cdot}CO$, 15·8%). The *benzoate* crystallised in needles from aqueous alcohol, m. p. 124—125° (Found: C, 75·7; H, 5·5. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4%). The *dibromo*-derivative, prepared with bromine (1 mol.) in cold benzene, crystallised from methanol in needles, m. p. 185—186°; light absorption: max., 207, 222, 331 mμ; log ε 4·42, 4·17, 4·17 (Found: C, 43·2; H, 3·8; Br, 40·1. $C_{14}H_{14}O_3Br_2$ requires C, 43·1; H, 3·6; Br, 41·0%). The *tribromo*-derivative prepared in acetic acid crystallised from methanol in plates, m. p. 176—178° (Found: C, 35·6; H, 3·0; Br, 50·8. $C_{14}H_{13}O_3Br_3$ requires C, 35·8; H, 2·8; Br, 51·1%); light absorption: max., 207, 224, 345 mμ; log ε 4·52, 3·91, 4·20.

7-*Demethyldihydrosuberosin.*—7-Demethylsuberosin (0·8 g.), shaken in ethanol (100 c.c.)

with palladium chloride (0·05 g.), absorbed hydrogen (1 mol.) at room temperature and pressure in 80 min. *7-Demethyldihydrosuberosin* separated in colourless needles, m. p. 106—108°, from benzene (Found: C, 72·4; H, 6·9. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%).

(±)*Nodakenetin* [(±)-*Marmesin*] (IX).—An ethereal solution of excess of monoperphthalic acid (3·3 g.) containing 7-demethylsuberosin (4 g.) was kept at 0° for 24 hr. Acidic material was then extracted with aqueous sodium hydrogen carbonate, and the residual solution was dried and evaporated. The residue of (±)-*nodakenetin* crystallised from benzene in glistening plates (2·4 g., 56%), m. p. 152—153° (Chatterjee and Mitra, *loc. cit.*, give the m. p. of an equimolecular mixture of nodakenetin and marmesin as *ca.* 155°) (Found: C, 68·3; H, 5·6. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). The compound was insoluble in cold alkalis, and unaffected by methylation with diazomethane or methyl sulphate–potassium carbonate, and by boiling with 20% sulphuric acid. The *acetate* (sodium acetate–acetic anhydride) crystallised from aqueous ethanol in elongated plates, m. p. 124—126° (*idem, loc. cit.*, give m. p. 130° for the acetates of the optically active compounds) (Found: C, 66·6; H, 5·3. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%).

Deoxyoreosolone (X).—(±)-Nodakenetin (0·25 g.) was heated with phosphoric oxide in benzene at the b. p. for 5 hr. and the benzene solution decanted, washed, and evaporated. The residual deoxyoreosolone (0·08 g.) crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 136—137° (*idem, loc. cit.*, give m. p. 138—140°) (Found: C, 73·3; H, 5·4. Calc. for $C_{14}H_{12}O_3$: C, 73·7; H, 5·3%).

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The Chemistry of Extractives from Hardwoods. Part XVII. The Occurrence of a Flavan-3 : 4-diol (Melacacidin) in* Acacia melanoxylon.

By F. E. KING and W. BOTTOMLEY.

[Reprint Order No. 4933.]

The amorphous material extracted by ether from Australian Blackwood (*Acacia melanoxylon*) consists largely of melacacidin, 3 : 4 : 7 : 8 : 3′ : 4′-hexahydroxyflavan, a compound of novel type characterised by crystalline derivatives. Its constitution has been demonstrated by oxidation of the tetramethyl ether, with potassium permanganate to 2-hydroxy-3 : 4-dimethoxybenzoic acid and veratric acid, and by the Oppenauer method to 7 : 8 : 3′ : 4′-tetramethoxyflavonol

As already briefly reported (King and Bottomley, *Chem. and Ind.*, 1953, 1368), melacacidin combines the properties of both leucoanthocyanidin and phlobatannin, thereby explaining the observations of Bate-Smith and Swain (*ibid.*, 1953, 377) and indicating a flavan-3 : 4-diol structure for this widely distributed group of natural products.

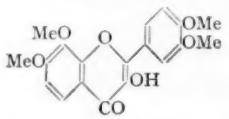
Acacia melanoxylon is a tree of medium size found in many parts of Australia and Tasmania, where it is of value as the source of a cabinet timber. A quantity of the heartwood procured through the kindness of the Conservator of Forests, Western Australia, has been investigated with respect to the nature of its extractable constituents. The only noteworthy product was a light amorphous powdery solid, amounting to approximately 1—1½% of the wood, phenolic in nature and largely soluble in cold water. No homogeneous compound was isolated from the extract nor were its various acylation products obtained crystalline. Nevertheless it is substantially a single compound and when treated with diazomethane it gave a crystalline optically active derivative, $C_{19}H_{22}O_7$, containing four methoxyl groups. Crude melacacidin was shown by Zeisel analysis to be methoxyl-free; hence the compound $C_{19}H_{22}O_7$ is melacacidin tetramethyl

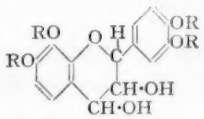
* Part XVI, preceding paper.

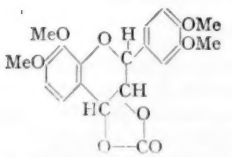
ether. The derivative exhibited no colour with ferric chloride and was insoluble in alkalis, but its formation of a diacetate indicated the presence of two alcoholic groups. Oxidation of the tetramethyl ether with potassium permanganate afforded a mixture of acids which were separated by conversion into methyl esters, one of them being phenolic and therefore alkali-soluble. The phenolic ester was identified as methyl 2-hydroxy-3 : 4-dimethoxybenzoate and the accompanying neutral ester as methyl veratrate.

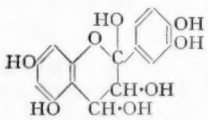
From the formation of these two oxidation products, one of them an *o*-hydroxy-acid, it seemed probable that melacacidin contained a dihydrodihydroxypyran nucleus. The ready oxidation of melacacidin tetramethyl ether with periodic acid proved that the two alcoholic substituents were present as an α-glycol unit; 2-hydroxy-3 : 4-dimethoxybenzaldehyde and an unidentified transformation product were isolated from this reaction, the former disclosing the position of the diol system with respect to the principal aromatic ring. Conclusive evidence as to the total structure of melacacidin was then obtained from an Oppenauer oxidation of the tetramethyl ether which yielded 7 : 8 : 3′ : 4′-tetramethoxyflavonol (I) (Kostanecki and Rudse, *Ber.*, 1905, **38**, 935), a sample of which was synthesised from 2-hydroxy-3 : 4 : 3′ : 4′-tetramethoxychalkone by oxidation with alkaline hydrogen peroxide. Melacacidin is therefore one of the stereoisomeric 7 : 8 : 3′ : 4′-flavan-3 : 4-diols represented as (II; R = H).

Methylation of the crude flavandiol with methyl sulphate–potassium carbonate in acetone for a limited time also resulted in a good yield of the tetramethyl ether (II; R = Me). Prolonged treatment under these conditions, on the other hand, gave a mixture of (II; R = Me) with two other crystalline products, one of them a pentamethyl compound [melacacidin 3(or 4) : 7 : 8 : 3′ : 4′-pentamethyl ether]. The identity of the remaining derivative, $C_{20}H_{20}O_8$, became apparent after it had been subjected to mild hydrolysis with

(I) 

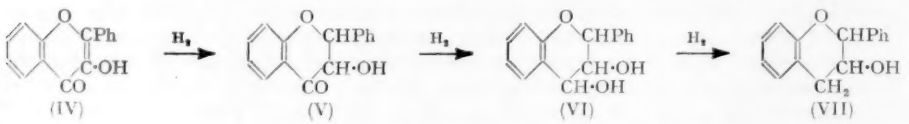
(II) 

(III) 

(VIII) 

alkali, the formation of the tetramethyl ether $C_{19}H_{22}O_7$ (II; R = Me) showing it to be a cyclic carbonate (III). This was afterwards confirmed by a synthesis of (III) from tetramethylmelacacidin and ethyl chloroformate in an aqueous alkaline medium. From the ready production of the cyclic carbonate (III) under the Robertson–Robinson methylation conditions it may be concluded that the diol system has the *cis*-configuration. The nature of this unusual reaction and also its possible application to other polyhydric compounds, *e.g.*, carbohydrates, appears to warrant further investigation.

Flavan-3 : 4-diols seem not to have been recognised hitherto as natural products, though closely related to the widely distributed series of flavonols. The discovery of melacacidin therefore completes the reduction sequence illustrated in prototype by the



(IV) (V) (VI) (VII)

structures (IV)—(VII) beginning with flavonols (type IV) and ending with the catechins (type VII), several flavanolones (type V) having in recent years been discovered in Nature (cf. Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031; Erdtman, "Progress in Organic Chemistry," Butterworth, ed. J. W. Cook, Vol. I, pp. 31, 37; Hillis, *Austral. J. Sci. Res.*, 1952, *A*, **5**, 379).

A structure resembling that of melacacidin, namely (VIII), was proposed by Robinson and Robinson (*Biochem. J.*, 1933, **27**, 206) for a leucoanthocyanidin, and the essential validity of their suggestion is clear from the properties of the amorphous extractive of *A. melanoxylon*, to which reference has been made in a preliminary publication (King and Bottomley, *Chem. and Ind.*, 1953, 1368). Thus heating it with mineral acid produces a deep scarlet solution similar to that of the anthocyanidins, although the amount of colouring matter generated is relatively small, the principal product being a red-brown amorphous material. Comparison with a synthetic specimen by means of paper chromatography, using acetic acid–butanol–water, has shown that the resulting anthocyanidin is the expected 3 : 7 : 8 : 3′ : 4′-pentahydroxyflavylium salt (Dr. J. W. Clark-Lewis, unpublished work). Although no natural anthocyanidin with the phenolic hydroxyl pattern of melacacidin has so far been encountered, in the light of observations by Bate-Smith and Swain (*Chem. and Ind.*, 1953, 377), who have concluded that the properties of so-called leucoanthocyanidins occurring in many plant products are indistinguishable from those of condensed tannins, the behaviour of melacacidin with acids is of considerable significance since it implies that the hitherto imperfectly defined " phlobatannins " also are derivatives of flavan-3 : 4-diol. Certain resemblances, *e.g.*, in ultra-violet light absorption, between the leucoanthocyanidins and catechins noted by Bate-Smith and Swain (*loc. cit.*) are therefore readily explained by the similarity of their structures, or may even be due to the actual conversion of the leucoanthocyanidins (in part) into catechins, as was recently demonstrated chromatographically by Forsyth (*Nature*, 1953, **172**, 726) in the case of cacao bean " leucoanthocyanin." The formation of a flavylium salt from the corresponding leucoanthocyanidin is an oxidation process and if it were to take place through a compensating reduction of the flavandiol to catechin the reason for the tannin reactions of the leucoanthocyanidins becomes obvious. On the other hand, the relatively small yield of anthocyanidin produced by the action of acids compared with that of the amorphous (presumed) polymer indicates that the mechanism of polymerisation is to a large degree independent of flavylium salt formation. Further investigation will no doubt show whether this new hypothesis as to the structure of phlobatannins or their precursors provides a satisfactory alternative to the flavpinacol theory due to Russell (*Chem. Reviews*, 1935, **17**, 155).

Evaporation of the ethereal solution remaining from the extraction of melacacidin gave an orange powder from which a small amount (0·01%) of 7 : 8 : 3′ : 4′-tetrahydroxyflavonol was obtained—the first indication of the natural occurrence of this compound.

Experimental

Melacacidin (II; R = H).—The ground heartwood of *A. melanoxylon* (2·8 kg.) was first extracted with boiling light petroleum and then for 3—4 days with ether, the metal extractor being heated on a steam-bath to avoid decomposition of the crude melacacidin which was deposited as a buff-coloured layer on the base of the vessel (yield, 28—45 g., 1—1·6%). The product was largely soluble in water, the simple alcohols, acetone, and acetic acid. Its aqueous solution gave a dark brown ferric reaction, and in boiling 10% hydrochloric acid a deep crimson solution from which gradually a brown precipitate separated. Both soluble and precipitated products were extracted into *iso*amyl alcohol to give deep red solutions. Melacacidin failed to give a crystalline acetate, benzoate, or *p*-nitrobenzoate; it was characterised by its methyl ethers (see below).

Melacacidin Tetramethyl Ether (3 : 4-*Dihydroxy*-7 : 8 : 3′ : 4′-*tetramethoxyflavan*) (II; R = Me).—(*a*) The crude extractive (1 g.) in methanol (10 c.c.) was treated with an ethereal solution of diazomethane and set aside overnight. Evaporation of the solvent under diminished pressure and crystallisation of the residue from ethanol yielded *tetramethylmelacacidin* (0·8 g.) as colourless needles, m. p. 145—146°, $[\alpha]_D$ −84·4° in EtOH (Found in a sample dried *in vacuo* at 100°: C, 63·1; H, 6·2; OMe, 33·6. $C_{19}H_{22}O_7$ requires C, 63·0; H, 6·1; 4OMe, 34·2%); light absorption: max., 217, 278 mμ; log ε 4·36, 3·39. Dissolved in hot alcoholic hydrogen chloride it gave a pale pink solution. *Tetramethylmelacacidin diacetate* crystallised from ethanol in needles, m. p. 193—194°, $[\alpha]_D$ −39·2° in EtOH (Found: C, 61·8; H, 5·9; OMe, 27·8; OAc, 20·2%; *M*, 456. $C_{23}H_{26}O_9$ requires C, 61·9; H, 5·9; 4OMe, 27·7; 2OAc, 19·3%; *M*, 446).

(*b*) A mixture of melacacidin (5 g.), potassium carbonate (35 g.), methyl sulphate (10 g.), and acetone (150 c.c.) was heated under reflux for 45 min. The filtered solution was then evaporated and the residue mixed with aqueous ammonia and set aside for several hours. The mixture was then acidified and the solid collected and crystallised from ethanol, melacacidin tetramethyl ether being obtained as needles (3 g.), m. p. 145—146°.

Tetramethylmelacacidin Carbonate (III).—(*a*) After the methylation of melacacidin (5 g.) with excess of methyl sulphate–potassium carbonate in acetone for 18 hr., the filtered liquid was evaporated to dryness and the residue mixed with benzene (20 c.c.). The insoluble solid, consisting of tetramethylmelacacidin, was removed, the solution evaporated, and the residue dissolved in boiling ethanol; *tetramethylmelacacidin carbonate* separated in needles, m. p. after recrystallisation, 209° (Found: C, 61·7; H, 5·4; OMe, 32·7%; *M*, 400. $C_{20}H_{20}O_8$ requires C, 61·85; H, 5·2; 4OMe, 31·9%; *M*, 388). A solution of the carbonate (0·1 g.) in acetone (5 c.c.) and N-aqueous sodium hydroxide (5 c.c.) was heated on a steam-bath until the acetone had evaporated. The solid collected from the cold solution crystallised from ethanol as needles, m. p. 145—146° alone or mixed with the compound (II; R = Me); it had $[\alpha]_D$ −84°.

(*b*) A mixture of tetramethylmelacacidin (0·1 g.) in acetone (4 c.c.) and water (4 c.c.) was treated with ethyl chloroformate (0·4 g.), and the solution made faintly alkaline with N-sodium hydroxide. After 10 min., alcohol (15 c.c.) was added, and when filtered from sodium chloride the solution was concentrated to *ca.* 10 c.c. The solid which was then collected crystallised from ethanol in needles, m. p. 209° alone or mixed with tetramethylmelacacidin carbonate.

Pentamethylmelacacidin [3(or 4)-*hydroxy*-4(or 3):7:8:3′:4′-*pentamethoxyflavan*] was isolated from the alcoholic solution remaining from the crystallisation of the carbonate (III) obtained by methylating melacacidin with methyl sulphate–potassium carbonate; it formed needles, m. p. 149°, from ethanol (Found: C, 63·7; H, 6·4; OMe, 39·8. $C_{20}H_{24}O_7$ requires C, 63·8; H, 6·4; 5OMe, 41·2%). Only the carbonate (III) and melacacidin pentamethyl ether were obtained after 48 hours' methylation of melacacidin.

Oxidation of Tetramethylmelacacidin with Potassium Permanganate.—A mixture of tetramethylmelacacidin (2 g.), potassium permanganate (3 g.), and acetone (100 c.c.) was heated under reflux for 4 hr. After the addition of water, the acetone was evaporated and the solution saturated with sulphur dioxide. Extraction with ether and shaking the ethereal solution with aqueous sodium hydrogen carbonate afforded a mixture of acids which was liberated from the carbonate solution, dissolved in ether, dried, and treated with excess of diazomethane. After 10 min. the solution was evaporated and the residue shaken with 2N-sodium hydroxide. The insoluble material consisted of methyl veratrate which when crystallised from alcohol had m. p. and mixed m. p. 59°.

The alkali-soluble ester was precipitated with hydrochloric acid and crystallised from aqueous methanol in prisms, m. p. 74—75° alone or mixed with synthetic methyl 2-hydroxy-3:4-dimethoxybenzoate. Hydrolysis of the ester with 2N-sodium hydroxide gave 2-hydroxy-3:4-dimethoxybenzoic acid, m. p. and mixed m. p. 170—171°.

Oxidation of Tetramethylmelacacidin with Periodic Acid.—The tetramethyl derivative (II; R = Me) (1 g.), dissolved in ethanol (20 c.c.), was treated with a solution of periodic acid (1·5 g.) in water (20 c.c.). After 4 hr., most of the alcohol was evaporated under diminished pressure and the residual liquid extracted with ether, which was washed in turn with aqueous sodium hydrogen carbonate and sodium hydroxide. Evaporation of the washed ethereal solution then yielded a semi-solid product from which was prepared a *semicarbazone*, m. p. 212°, alone or mixed with 2-hydroxy-3:4-dimethoxybenzaldehyde semicarbazone (Found: C, 50·2; H, 5·7; N, 17·6; OMe, 25·2. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·5; N, 17·6; 2OMe, 25·9%).

The material isolated from the sodium hydroxide extract was redissolved in ether and again shaken with alkali. Acidification of the alkaline solution and ether-extraction yielded a substance crystallising from aqueous methanol in prisms, m. p. 103°, no longer soluble in sodium hydroxide and showing no reaction with ferric chloride (Found: C, 67·9; H, 5·7; OMe, 41·3%; *M*, 306).

Oppenauer Oxidation of Tetramethylmelacacidin.—To a solution of melacacidin (2 g.) in toluene (45 c.c.), prepared by concentrating a more dilute solution, *cyclo*hexanone (12 c.c.) and a saturated solution of aluminium *tert.*-butoxide in toluene (20 c.c.) were added and the mixture was heated under reflux for 1½ hr. It was then treated with water, acidified, and steam-distilled to remove solvent, etc., after which the residual solid was collected and crystallised from acetic acid. 7:8:3′:4′-Tetramethoxyflavonol (I) was thus obtained as small yellow prisms (0·4 g.), m. p. 220—221° alone or mixed with the synthetic specimen (Found: C, 63·4; H, 5·2. Calc. for $C_{19}H_{18}O_7$: C, 63·7; H, 5·1%). The acetate, needles from methanol,

had m. p. and mixed m. p. 174—175° (Found : C, 63·1; H, 4·8. Calc. for $C_{21}H_{20}O_8$: C, 63·0; H, 5·0%).

Synthesis of 7 : 8 : 3′ : 4′-*Tetramethoxyflavonol* (cf. Kostanecki and Rudse, *loc. cit.*).—2-Hydroxy-3 : 4 : 3′ : 4′-tetramethoxychalkone (Crabtree and Robinson, *J.*, 1922, **121**, 1033) (5 g.) was dissolved in 50% aqueous ethanol (100 c.c.) containing sodium hydroxide (10 g.) to which 30% hydrogen peroxide (10 c.c.) was then added. During the first exothermic reaction the mixture was cooled and then set aside at room temperature for 1 hr. When the crystalline slurry had been acidified, 7 : 8 : 3′ : 4′-tetramethoxyflavonol was collected and crystallised from acetic acid, to give yellow prisms, m. p. 220—221° (Found : C, 63·5; H, 5·0; OMe, 34·7%); the acetate formed needles, m. p. 174—175° (Found : C, 63·1; H, 4·8; OMe, 30·5%).

Isolation of 7 : 8 : 3′ : 4′-*Tetrahydroxyflavonol.*—After being decanted from the deposit of melacacidin, the ethereal solution from the extraction of 15 kg. of the wood was evaporated and the residue heated in boiling water (200 c.c.). The boiling liquid was filtered and the insoluble residue (1·7 g.) washed with a little hot acetic acid and crystallised from ethanol. 7 : 8 : 3′ : 4′-Tetrahydroxyflavonol was isolated as yellow blades, m. p. (decomp.) *ca.* 312—320° (Found : C, 59·2; H, 3·6. Calc. for $C_{15}H_{10}O_7$: C, 59·6; H, 3·3%).

Methylation with methyl sulphate–potassium carbonate in acetone for 20 min. gave 7 : 8 : 3′ : 4′-tetramethoxyflavonol, m. p. and mixed m. p. 220—221° (acetate, m. p. and mixed m. p. 174—175°). Continued methylation under these conditions yielded 3 : 7 : 8 : 3′ : 4′-pentamethoxyflavone as needles, m. p. 151° alone or with a synthetic specimen. Row, Seshadri, and Thiruvengadam (*Proc. Indian Acad. Sci.*, 1948, **28**, A, 98) give m. p. 153—154° (Found : C, 64·5; H, 5·1; OMe, 40·8. Calc. for $C_{20}H_{20}O_7$: C, 64·5; H, 5·4; 5OMe, 41·6%).

THE UNIVERSITY, NOTTINGHAM. [*Received, December 28th*, 1953.]

Triterpene Acids from the Leaves of Psidium guaijava, *L.*

By H. R. ARTHUR and (MISS) W. H. HUI.

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" Psidiolic acid," isolated from the leaves of *Psidium guaijava*, L., and previously reported as a new triterpene acid, has been shown to be a mixture containing ursolic acid, oleanolic acid, crategolic acid, and a new triterpene acid which we have named guaijavolic acid. Guaijavolic acid, $C_{30}H_{48}O_4$, contains a tertiary carboxyl group and two hydroxyl groups.

SOLIMAN and FARID (*J.*, 1952, 134) reported that they had isolated from the leaves of *Psidium guaijava*, L. (Myrtaceae) a new triterpene acid which they called " psidiolic acid," and we showed (*Chem. and Ind.*, 1952, 693) that the leaves of the local species of *Psidium guaijava* also contained " psidiolic acid." Our material, which separated from organic solvents in spheroidal aggregates and gave a reddish-violet colour in the Liebermann–Burchardt test, had m. p. 254—256°; and the m. p.s of its derivatives corresponded with those stated by Soliman and Farid. Because of the manner in which " psidiolic acid " separated from organic solvents, we believed that it was a mixture.

A sample of " psidiolic acid " was chromatographed on alumina. Development for 80 hr. with acetone followed by elution with ethyl acetate, gave 65 fractions, the first 23 of which consisted almost entirely of ursolic acid. The more soluble oleanolic acid was obtained in very low yield from the filtrates of the fractions containing ursolic acid.

Fractions 26—65 contained a triterpenoid substance (*A*) which separated from aqueous ethanol in clusters of short needles. Microscopic examination of (*A*) after it had separated from ethanol or methanol showed that it was obtainable in the form of " threads " (or " rods "), " arrow heads," or " spheres " thus giving evidence of a metastable mesomorphic state (J. Alexander, " Colloid Chemistry," Vol. 1, Chemical Catalog Co. Inc., New York) 1926). While " psidiolic acid " gives a reddish-violet colour in the Liebermann–Burchardt test, and ursolic acid and oleanolic acid a red ⟶ violet ⟶ blue ⟶ green colour, (*A*, gave a red ⟶ orange-red colour.

Because (*A*) could be obtained crystalline only with difficulty, a mixture was again suspected. A sample of (*A*) was chromatographed on alumina, but no change in properties of any of the fractions was observed. It sublimed unchanged in a high vacuum at 200°; a sample was acetylated and the product chromatographed on alumina by two different procedures, one with petroleum and chloroform, and the other with acetone and ethyl acetate; but neither procedure effected a separation.

However, fractional recrystallisation of the acetate of (*A*) from light petroleum (b. p. 40—60°), a triangular scheme being used, gave after 5 operations the least soluble fraction as fine needles, the m. p. of which could not be raised by further recrystallisation or by chromatography. Hydrolysis of this acetate yielded a new crystalline acid (*B*), $C_{30}H_{48}O_4$, which we have called guaijavolic acid; that it contains a tertiary carboxyl group was shown by titration with alkali and by the preparation of a methyl ester which resists hydrolysis with ethanolic alkali. The presence of two hydroxyl groups was shown by the formation of the diacetate and the methyl ester dipropionate. The acid gives a yellow colour with tetranitromethane and the usual colour reactions characteristic of triterpenoid compounds.

The fraction of the acetate of (*A*) which was more soluble in light petroleum than guaijavolic acid diacetate could not be obtained pure from a repetition of the fractional recrystallisation. When hydrolysed it yielded an acid which melted over a range at about 270°. The methyl ester of this acid, however, gave on fractional recrystallisation from light petroleum (b. p. 40—60°) a product (*C*) which had m. p. 221—223°, alone or on admixture with authentic methyl crategolate. The authentic methyl crategolate was obtained from the leaves of *Crataegus oxyacantha*, L. (Rosaceae) and purified by Tschesche, Heesch, and Fugmann by the method described by them (*Chem. Ber.*, 1953, **86**, 626). The identity of (*C*) with methyl crategolate was finally established by reference to their infra-red absorption spectra.

Tschesche and Fugmann (*ibid.*, 1951, **84**, 810) isolated from the leaves of *Crataegus oxyacantha* an intimate mixture of triterpenoid acids, which they called *cis*- and *trans*-crategolic acids; they considered that crategolic acid was 2 : 19-dihydroxyurs-13(18)-ene-17-carboxylic acid. However, Bersin and Muller (*Helv. Chim. Acta*, 1951, **34**, 1868) showed that the leaves of this plant contained ursolic acid, of which the former workers made no mention. In a second paper (*ibid.*, 1952, **35**, 1891), Bersin and Muller showed that oleanolic acid was also present.

It was shown by Tschesche, Heesch, and Fugmann (*loc. cit.*) that Tschesche and Fugmann's "crategolic acid" contained 60—65% of ursolic acid, since methyl ursolate could be chromatographically removed from the methyl esters of the triterpenoid mixture; the residue gave, on repeated recrystallisation, methyl crategolate identical (m. p., mixed m. p., and infra-red spectrum) with (*C*) obtained by fractional recrystallisation of the methyl esters of the triterpenoid mixture from the leaves of *Psidium guaijava* after removal of ursolic, oleanolic, and guaijavolic acids.

The molecular formula and structure of crategolic acid need elucidation since Tschesche and Fugmann's work (*loc. cit.*) was carried out on material containing a large proportion of ursolic acid. Analysis of purified samples of methyl crategolate from *Crataegus oxyacantha* and *Psidium guaijava* suggest that crategolic acid is a monocarboxylic acid of the formula $C_{30}H_{48}O_4$, as originally suggested by Tschesche and Fugmann, and is possibly isomeric with guiajavolic acid.

There is a similarity in the triterpenoid constituents of both plants since they contain in common, ursolic acid, oleanolic acid, and crategolic acid. It is possible that the leaves of *Crataegus oxyacantha* also contain guaijavolic acid, since Bersin and Muller have shown that the triterpenoid mixture from that plant contains 30·2% of ursolic acid, 2·1% of oleanolic acid, and 40·0% of a mixture not separated. Whilst the yield of the triterpenoid mixture from *Crataegus oxyacantha* is 25%, that from *Psidium guaijava* is 0·7%. We have shown that the mixture from the latter contains 33% of ursolic acid, 1·5% of oleanolic acid, 12% of guaijavolic acid, and 10% of crategolic acid.

Guaijavolic acid diacetate and methyl guaijavolate, after recrystallisation to constant m. p., showed no change in properties when chromatographed. Samples of guaijavolic acid

obtained by the hydrolysis of the diacetate before and after chromatography of the diacetate were identical.

Experimental

M. p.s are corrected. Some analyses are by Dr. Zimmermann, Melbourne. Mixed m. p.s with authentic specimens were determined with ursolic acid and oleanolic acid and their derivatives. No depressions were observed. The alumina used for chromatography was B.D.H., analysis grade. Spectra were measured on a Grubb-Parsons S3A spectrometer equipped with a sodium chloride prism; solutions were in carbon disulphide.

Dried powdered leaves (3 kg.) of *Psidium guaijava* were extracted for 60 hr. with petroleum (b. p. 60—80°) and then with cold ether (3 × 10 l.). The ethereal extract was shaken twice with an equal volume of sodium hydroxide solution (1%). On acidification, the brown alkaline extract yielded a green precipitate (45 g.) which after six crystallisations from ethanol (charcoal) yielded white spheroidal aggregates (20 g.), m. p. 254—256°. Attempts to crystallise this mixture from polar and non-polar organic solvents failed. The mixture (10 g.) was dissolved in acetone and chromatographed on alumina (1 kg.); development for 80 hr. with acetone was followed by elution with ethyl acetate. Each fraction (400 ml.) was evaporated to dryness, and the residues were dissolved in ethanol and left to crystallise.

Ursolic Acid.—Fractions 1—23 deposited needles (3 g.) of ursolic acid which after two recrystallisations had m. p. 290—291° (vac.), $[\alpha]_D^{21}$ +67° (*c*, 1·07 in 1 : 1-methanol–chloroform) (Liebermann–Burchardt test: a red ⟶ violet ⟶ blue ⟶ green) (Found: C, 78·7; H, 10·5. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). It formed ursolic acid acetate, m. p. 293—295° (Found: C, 77·0; H, 9·8. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%), methyl ursolate, m. p. 170° (Found: C, 79·5; H, 10·9. Calc. for $C_{31}H_{50}O_3$: C, 79·1; H, 10·7%), and methyl ursolate acetate, m. p. 246—247° (Found: C, 77·3; H, 10·2. Calc. for $C_{33}H_{52}O_4$: C, 77·3; H, 10·2%). Hydrolysis of ursolic acid acetate (by ethanolic potassium hydroxide) and of methyl ursolate (by potassium hydroxide in ethylene glycol) yielded ursolic acid, m. p. 290—291° (vac.).

Oleanolic Acid.—Five crops of ursolic acid were removed from fractions 1—23. The sixth crop, which was amorphous and had m. p. higher than ursolic acid, yielded after two crystallisations from ethanol, oleanolic acid (0·15 g.) as needles, m. p. 310—312° (vac.) (Liebermann–Burchardt test: red ⟶ violet ⟶ blue ⟶ green). It formed methyl oleanolate, m. p. 201° (Found: C, 79·1; H, 10·6; OMe, 6·4. Calc. for $C_{31}H_{50}O_3$: C, 79·1; H, 10·7; OMe, 6·6%), and methyl oleanolate acetate, m. p. 219—221°.

Guaijavolic Acid.—Fractions 27—65 [substance (*A*)] (5 g.), obtained by chromatography, had identical properties; fractions 24—26 were mixtures of ursolic, oleanolic, crategolic and guaijavolic acids. Substance (*A*) (Liebermann–Burchardt test: red ⟶ orange-red ⟶ brown) crystallised from aqueous ethanol, from which it separated in clusters of short needles, but did not crystallise from other solvents. Despite repeated recrystallisation and sublimation, m. p.s were variable, ranging from 250° to 270° in open tubes. It had m. p. 290° (vac.) after softening at 255—260°, before or after re-chromatography on alumina.

The acetate of (*A*), after being boiled for an hour in 70% aqueous ethanol in order to decompose mixed anhydrides, did not give a sharp m. p., nor could the m. p. be improved by two different chromatographic procedures. It (5 g.) was fractionally recrystallised from light petroleum (b. p. 40—60°), a triangular scheme being used. The least soluble fraction (1·2 g.) was obtained as fine needles, m. p. 242—244°, not raised by recrystallisation or by chromatography. This was *guaijavolic acid diacetate*, $[\alpha]_D^{22}$ +20·7° (*c*, 1·11 in $CHCl_3$) (Found: C, 73·0; H, 9·0; Ac, 15·4. $C_{34}H_{52}O_6$ requires C, 73·3; H, 9·4; 2Ac, 15·5%), which was hydrolysed by ethanolic potassium hydroxide to *guaijavolic acid* (*B*), m. p. 306—308° (vac.) (from aqueous ethanol), $[\alpha]_D^{22}$ +34·4° (*c*, 0·62 in C_5H_5N) [Found: C, 75·8; H, 10·2%; equiv., 454 (by titration); *M*, 487. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2%; equiv., 472 (for one carboxyl group); *M*, 472]. It gave a pale yellow colour with tetranitromethane and a red ⟶ orange-red ⟶ brown colour in the Liebermann–Burchardt test. Treatment of guaijavolic acid with ethereal diazomethane gave *methyl guaijavolate*, which crystallised from light petroleum in needles, m. p. 210—211°, $[\alpha]_D^{17}$ +55° (*c*, 0·25 in $CHCl_3$) (Found: C, 76·6; H, 10·2; OMe, 6·3. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4; OMe, 6·4%). *Methyl guaijavolate dipropionate* was prepared by dissolving the methyl ester (0·6 g.) in a mixture of pyridine (4 ml.) and propionic anhydride (4 ml.). The mixture was left for 3 days at room temperature and then poured into water. The product crystallised from ethanol (charcoal) in prisms, m. p. 154—155° (Found: C, 74·5; H, 9·8; OMe, 5·2. $C_{37}H_{58}O_6$ requires C, 74·2; H, 9·8; OMe, 5·2%).

Methyl Crategolate.—All fractions of the more soluble acetylated (*A*) had a m. p. range of several degrees, and a repetition of the fractional crystallisations by processes similar to that which yielded guaijavolic acid diacetate produced nothing of constant m. p. This material (1·9 g.) was hydrolysed and the free acids were converted by means of diazomethane into the methyl esters which were fractionally recrystallised from light petroleum (b. p. 40—60°). The least soluble fraction (1·0 g.) was obtained as fine needles, m. p. 221—223° alone or in admixture with a sample of purified methyl crategolate obtained from Professor Tschesche (Found: C, 76·8; H, 10·4; OMe, 6·3. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·4; OMe, 6·4%). Both samples of methyl crategolate gave identical infra-red spectra in the range 900—1350 cm.$^{-1}$.

The more soluble methyl esters had a m. p. range, as had the more soluble acetates. These fractions were considered to be mixtures of the methyl esters and the acetates of guaijavolic acid and crategolic acid.

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UNIVERSITY OF HONG KONG, HONG KONG. [*Received, January 5th*, 1954.]

The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part I. Ethylene Glycol.

By G. J. BUIST and C. A. BUNTON.

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The kinetics of oxidation of ethylene glycol by periodic acid have been studied in aqueous solution, at 0°, over a wide range of pH. The kinetic form shows that an intermediate complex is formed in high concentration, in equilibrium with the glycol and periodic acid, and allows the determination of equilibrium and rate-coefficients for the formation of the complex, and its decomposition. The effect of pH on these coefficients shows that the decomposing entity is $(CH_2{\cdot}O)_2IO_4H_2^-$ or its dehydrated species $(CH_2{\cdot}O)_2IO_3^-$.

THE kinetics of the oxidation of α-glycols by periodic acid in aqueous solution have been studied by Price and his co-workers (*J. Amer. Chem. Soc.*, 1938, **60**, 2726; 1942, **64**, 552) for several compounds over a range of pH; they observed the marked effect of acidity on reaction rate. A careful study of the effect of reactant concentration on rate was made by Duke (*ibid.*, 1947, **69**, 3054), in the oxidation of ethylene glycol; this system has been further investigated by Taylor (*ibid.*, 1953, **75**, 3912). Duke's results were found to obey the equation

$$k' \propto [G]/(1 + K[G])$$

where k' is the first-order rate coefficient with respect to periodic acid, [G] is the concentration of ethylene glycol, and K is a constant. This relation was explained in terms of a rapid reversible formation of an intermediate between the glycol and periodic acid, followed by slow decomposition of the intermediate:

$$\begin{matrix}CH_2{\cdot}OH\\CH_2{\cdot}OH\end{matrix} + H_5IO_6 \overset{K}{\rightleftharpoons} \text{Intermediate} \xrightarrow[\text{(slow)}]{k} 2CH_2O + HIO_3 + 2H_2O$$

This reaction sequence requires the kinetic law

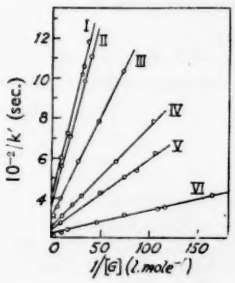
$$k' = kK[G]/(1 + K[G]),\ \textit{i.e.},\ 1/k' = 1/kK[G] + 1/k \quad . \quad . \quad . \quad (a)$$

The results gave values for the equilibrium constant K and the rate coefficient k, for the formation and decomposition, respectively, of the intermediate, and showed that the equilibrium was heavily in favour of the intermediate.

However, since under his conditions ([periodic acid] in aqueous solution = 0·008M) Duke observed no effect of acidity on rate, it appeared that a systematic study of the effects of both acidity and reactant concentration might give evidence for the nature of the intermediate and its mode of decomposition.

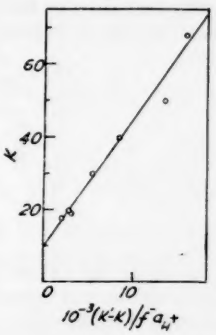
The oxidation of ethylene glycol, in aqueous periodic acid at 0°, was studied over a pH range 1—9, with wide variations of reactant concentrations and ionic strength (Buist, Bunton, and Shiner, *Research*, 1953, **6**, 45). The relation deduced by Duke (*loc. cit.*) was confirmed over this range of acidity. Furthermore, it was found that both the equilibrium constant K and the rate coefficient k were dependent upon acidity and upon ionic

FIG. 1. *Examples of dependence of first-order rate constant on concentration of ethylene glycol.*



I, pH = 1·14; I = 0·08
I , pH = 1·14; I = 0·13
III, pH = 1·45; I = 0·03
IV, pH = 1·94; I = 0·01
V, pH = 1·98; I = 0·13
VI, pH = 4·34; I = 0·13

FIG. 2. *Dependence of equilibrium constant on acidity.*



strength I. Examples of the values obtained are given in Table 1, and the data from which they are obtained are illustrated in Fig. 1.

Observations on the change of pH during the reaction suggest the cause of this dependence. When an excess of the glycol is added to a periodic acid solution at pH 2 an immediate drop in pH occurs, followed by a slow decrease, due to the decomposition of the intermediate, with formation of the relatively strong iodic acid. This initial drop in pH shows that the intermediate is a stronger acid than periodic acid. A similar experiment at pH 5 gives a similar initial drop in pH, followed by a slow *increase*. This

TABLE 1. *Effect of* pH *and ionic strength on* k *and* K.

pH	0·96	1·13	1·15	1·45	1·61	1·94	1·98	3·05	4·34	4·34
I (mole l.$^{-1}$) ...	0·134	0·084	0·134	0·03	0·134	0·01	0·134	0·134	0·134	0·021
10^3k (sec.$^{-1}$) ...	20·3	24·8	27·9	33·0	36·8	39·5	41·7	45·1	45·5	45·9
K (l. mole^{-1}) ...	17·7	19·5	18·7	30·1	40	50	68	141	189	196
pH	5·25	6·23	6·76	7·01	7·01	7·30	7·68	9·19	9·58	
I (mole l.$^{-1}$) ...	0·05	0·065	0·09	0·030	0·129	0·123	0·12	0·130	0·130	
10^3k (sec.$^{-1}$) ...	44·0	32·8	18·5	16·5	11·6	6·94	2·73	0·070	0·030	
K (l. mole^{-1}) ...	188	237	345	476	540	—	~1000	—	~2500	

increase, during the decomposition of the intermediate, must be due to the replacement of doubly-negatively charged ions by singly-negatively charged iodate ions. Since kinetic data show that *ca.* 95% of the periodic acid is combined under these conditions, these doubly-negatively charged ions must be derived from the glycol–periodate complex, and not simply from the periodic acid. Examples of the change of pH with time are given in Table 2.

TABLE 2.

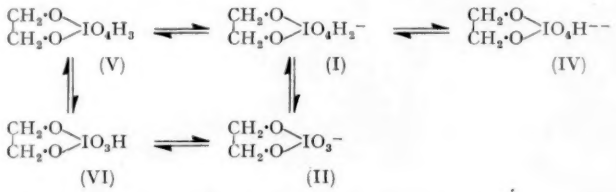
Aqueous solution, 0°. Glycol = 0·05M. Periodate = 0·01M.

(*a*) Time (sec.) ...	0	20	80	200	420	800	1080	1260		
pH	2·36	2·23	2·17	2·15	2·13	2·11	2·11	2·11		
(*b*) Time (sec.) ...	0	30	125	215	320	550	840	1150	1380	1680
pH	5·11	4·55	4·62	4·72	4·83	5·10	5·40	5·62	5·70	5·75

In considering an interpretation of the rate data, we must consider not only the equilibria between the various species of periodic acid, *viz.*,

$$H_5IO_6 \rightleftharpoons H^+ + H_4IO_6^- \rightleftharpoons IO_4^- + 2H_2O$$
$$\Updownarrow$$
$$H^+ + H_3IO_6^{--}$$

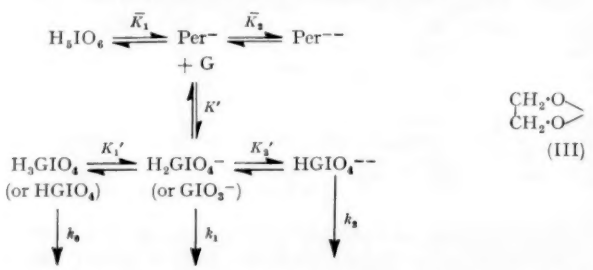
and the effect of acidity on these equilibria (Crouthamel *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 82), but also the related equilibria between the various intermediate species, which are formed by the co-ordination of a glycol molecule with periodic acid or its ions:



In so far as the dehydrated species have the same charge as their precursors, they must show a similar pH dependence, and our rate data do not differentiate between intermediate species of the same charge formed between one molecule of a glycol and one of a periodic acid.

The effect of pH on the equilibrium constant between ethylene glycol and periodic acid, all species of periodic acid and the intermediate complex being considered, can be predicted qualitatively from the fact that the co-ordinated glycol complex is a stronger acid than periodic acid, and therefore the equilibrium constant increases with increasing pH (cf. Table 1). A prediction of the effect of pH on the rate of decomposition of the intermediate cannot be made on such a simple basis, and requires detailed consideration of all the possible reactions involved. In principle, any of the intermediates may decompose to give the products of reaction, but, as will be shown, the only decomposing entity is the singly-charged ion (I) or its dehydrated species (II).

Nature of Reacting Species, and Dependence on Acidity.—The possible reactions involved in the formation and decomposition of the intermediates are



where G represents the residue (III) and Per^- and Per^{--} represent the totality of singly- and doubly-negatively charged periodate ions respectively. In so far as the periodate and intermediate complex species are in equilibrium, we have no evidence for the actual route of formation of the intermediates, and use the above formulation for convenience in

calculation. Taylor (*loc. cit.*) has put forward thermodynamic arguments to show that IO_4^- is the reactive species in the formation of the intermediate. The reasoning is erroneous since thermodynamic data alone can give no evidence for the mechanism of a kinetic process.

The apparent first and second ionisation constants of periodic acid, $\bar{K}_1$ and $\bar{K}_2$, are given by

$$\bar{K}_1 = \frac{f^-\{[H_4IO_6^-] + [IO_4^-]\}a_{H^+}}{[H_5IO_6]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\bar{K}_2 = \frac{f^{=}a_{H^+}[Per^{--}]}{f^-\{[H_4IO_6^-] + [IO_4^-]\}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where f^z is the activity coefficient of the z-charged periodate ions and f^z_i used below is that of the z-charged intermediate complex ions.

The experimentally observed equilibrium constant, K, and rate coefficient, k, are calculated from the kinetic data by equation (*a*) (p. 1406).

Now $$K = [\text{Total intermediate}]/[\text{Glycol}][\text{Total periodate}] \quad . \quad . \quad . \quad (3)$$

i.e., $$K = \frac{[H_3GIO_4] + [H_2GIO_4^-] + [HGIO_4^{--}]}{[\text{Glycol}]\{[H_5IO_6] + [Per^-] + [Per^{=}]\}} \quad . \quad . \quad . \quad . \quad (3a)$$

Similarly, we can consider the equilibria between the intermediates :

$$[H_3GIO_4] = a_{H^+}[H_2GIO_4^-]f_i^-/K_1' \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and $$[HGIO_4^{=}] = K_2'[H_2GIO_4^-]f_i^-/a_{H^+}f_i^{=} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

We do not in these equations differentiate between the hydrated and dehydrated intermediate species, and the activity coefficients for all neutral species are assumed equal to unity.

These expressions give

$$K = \frac{[H_2GIO_4^-]\left\{1 + \frac{f_i^-a_{H^+}}{K_1'} + \frac{f_i^-K_2'}{f_i^{=}a_{H^+}}\right\}}{[\text{Glycol}]\left\{1 + \frac{f^-a_{H^+}}{\bar{K}_1} + \frac{f^-\bar{K}_2}{f^{=}a_{H^+}}\right\}[Per^-]} = K'\left\{\frac{1 + \frac{f_i^-a_{H^+}}{K_1'} + \frac{f_i^-K_2'}{f_i^{=}a_{H^+}}}{1 + \frac{f^-a_{H^+}}{\bar{K}_1} + \frac{f^-\bar{K}_2}{f^{=}a_{H^+}}}\right\} \quad . \quad (6), (7)$$

since $K' = [H_2GIO_4^-]/[\text{Glycol}][Per^-]$

The total rate of decomposition of the intermediate is given by

$$k[C] = k_0[H_3GIO_4] + k_1[H_2GIO_4^-] + k_2[HGIO_4^{=}] \quad . \quad . \quad . \quad . \quad (8)$$

where k_0, k_1, and k_2 are the respective first-order rate coefficients for the decomposition of the various species, and [C] is the total concentration of the intermediates. Therefore

$$k[C] = [H_2GIO_4^-]\left\{\frac{k_0a_{H^+}}{K_1'}f_i^- + k_1 + \frac{k_2K_2'}{a_{H^+}}\frac{f_i^-}{f_i^{=}}\right\} \quad . \quad . \quad . \quad . \quad (8a)$$

but $[C] = [H_3GIO_4] + [H_2GIO_4^-] + [HGIO_4^{--}]$

$$= [H_2GIO_4^-]\left\{\frac{a_{H^+}}{K_1'}f_i^- + 1 + \frac{K_2'}{a_{H^+}}\cdot\frac{f_i^-}{f_i^{=}}\right\}$$

$$\therefore \quad k = \frac{k_1 + \frac{k_0a_{H^+}}{K_1'}f_i^- + \frac{k_2K_2'}{a_{H^+}}\frac{f_i^-}{f_i^{=}}}{1 + \frac{a_{H^+}}{K_1'}f_i^- + \frac{K_2'f_i^-}{a_{H^+}f_i^{=}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Reactions in Solutions of pH > 5.—Preliminary measurements of the change of pH in aqueous solutions of periodic acid and ethylene glycol show that the first ionisation

constant, K_1', for the intermediate is not less than 2×10^{-2}, and so $a_{H^+}/K_1' \ll 1$; also as the apparent first ionisation constant of periodic acid, $\overline{K}_1$, is $\sim 4 \times 10^{-3}$, $a_{H^+}/\overline{K}_1 \ll 1$.

We assume that k_0, k_1, and k_2 are independent of pH and ionic strength, and we can therefore express the rate coefficient k in terms of k_1 and k_2 (at this high pH we neglect the undissociated intermediate species):

$$k = \left\{k_1 + \frac{k_2 K_2'}{a_{H^+}} \cdot \frac{f_i^-}{f_i^{=}}\right\} \Big/ \left\{1 + \frac{K_2'}{a_{H^+}} \cdot \frac{f_i^-}{f_i^{=}}\right\} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

If we assume that $k_2 \sim 0$, (10) reduces to

$$k = \{k_1 a_{H^+} f_i^{=}/f_i^-\}/\{K_2' + a_{H^+} f_i^{=}/f_i^-\} \quad . \quad . \quad . \quad . \quad . \quad (10a)$$

Equation (10*a*) allows a test of the validity of these assumptions to be made by plotting $1/k$ against $f_i^-/a_{H^+} f_i^{=}$. To allow an assignment of numerical values to a_{H^+}, f_i^-, and $f_i^{=}$, we assume that a glass electrode gives a measure of the hydrogen-ion activity, *i.e.*, that pH $= -\log_{10} a_{H^+}$, and that the activity coefficients f_i^- and $f_i^{=}$, for the singly- and doubly-negatively charged intermediate ions, can be calculated from the expression $-\log f^2 = 0{\cdot}486 z^2 \sqrt{I}/(1 + \sqrt{I})$. The first assumption, in effect, requires the liquid-junction potential to be constant in the range of pH considered.

The very large change of hydrogen-ion activity in the pH range 5—9 renders this test somewhat insensitive in its present form over this whole range. The test, however, indicates that $k_2 \sim 0$, *i.e.*, that the doubly-negatively charged intermediate species does not decompose, and gives the following values for the rate coefficient, k_1, of the singly-negatively charged intermediate, and its ionisation constant, K_2':

$$k_1 = 45{\cdot}7 \times 10^{-4} \text{ sec.}^{-1}; \; K_2' = 1{\cdot}16 \times 10^{-7} \text{ mole l.}^{-1}$$

More precise values for these quantities are derived later.

Reactions in Solutions of pH <5.—The approximate value obtained above for K_2' allows us to neglect the presence of the doubly-negatively charged intermediate in solutions of pH <5. With this simplification, equation (9) reduces to

$$k = \left\{k_1 + f_i^- \cdot \frac{a_{H^+}}{K_1'} \cdot k_0\right\} \Big/ \left\{1 + \frac{a_{H^+}}{K_1'} \cdot f_i^-\right\} \quad . \quad . \quad . \quad . \quad . \quad (11)$$

i.e.,
$$1/k = 1/k_1 + f_i^- a_{H^+}/K_1' k_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad (11a)$$

if the term including k_0 is negligible compared with k_1 in the pH range studied. Again we make the approximations which allow numerical values to be assigned to a_{H^+} and f_i^-.

In Table 3 are given values of $f_i^- a_{H^+}$ and of the corresponding calculated and observed values of $1/k$; the agreement shows that equation (11*a*) is obeyed, *i.e.*, that k_0 is small or zero, and allows a value of $7{\cdot}4 \times 10^{-2}$ mole l.$^{-1}$ to be assigned to K_1'. The estimated value of k_1 is $45{\cdot}7 \times 10^{-4}$ sec.$^{-1}$.

TABLE 3. *Dependence of rate constant on hydrogen-ion activity.*

pH	I	$10^3 f_i^- a_{H^+}$	$1/k$ (calc.) (sec.)	$1/k$ (obs.) (sec.)	pH	I	$10^3 f_i^- a_{H^+}$	$1/k$ (calc.) (sec.)	$1/k$ (obs.) (sec.)
4·33	0·134	0·034	219	218	1·45	0·03	30·2	308	303
3·05	0·134	0·67	221	222	1·15	0·134	53·3	377	358
1·98	0·134	7·8	242	240	1·13	0·084	57·6	389	403
1·94	0·01	10·4	250	253	0·95	0·134	84·5	469	492
1·61	0·134	18·2	273	272					

By similar considerations we can use the experimental data obtained in solutions of pH <5 to obtain numerical values for the constants of the equilibria involved. In this acidity range we can neglect K_2' and $\overline{K}_2$, and equation (7) reduces to

$$K = K'\left\{1 + f_i^- \frac{a_{H^+}}{K_1'}\right\} \Big/ \left\{1 + f^- \cdot \frac{a_{H^+}}{K_1}\right\} \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Using the experimentally determined values in equation (7), we find that $K = K'$ at pH = 4·3; this allows us to assign a numerical value to K'. We further assume that the activity coefficients f^- and f_i^- for the singly-negatively charged periodate and intermediate ions are equal. Then equation (12) rearranges to

$$K = \frac{\bar{K}_1(K' - K)}{f^- a_{H^+}} + \frac{K'\bar{K}_1}{\bar{K}_1'} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12a)$$

and we can plot K against $(K' - K)/f^- a_{H^+}$. Again we make the previously mentioned approximations to the values of a_{H^+} and f^-. This graphical plot is shown in Fig. 2.

The values estimated from Fig. 2 are: (*a*) $\bar{K}_1 = 3{\cdot}6 \times 10^{-3}$, which can be compared with the values obtained by Crouthamel *et al.* (*loc. cit.*) by ultra-violet absorption spectrophotometry, of 4×10^{-3}, and that from buffer measurements of $4{\cdot}0 \times 10^{-3}$; and (*b*) $K_1' = 6{\cdot}8 \times 10^{-2}$, comparing well with the value $7{\cdot}4 \times 10^{-2}$ obtained by consideration of the effect of acidity on the rate of decomposition of the intermediate complex.

For results in alkaline solution we have the approximate value $45{\cdot}7 \times 10^{-4}$ sec.$^{-1}$ for k_1, and $1{\cdot}16 \times 10^{-7}$ for the second dissociation constant of the intermediate complex.

We know also that the singly-negatively charged intermediate is the only decomposing entity under our experimental conditions, and with these simplifications it is possible to use the data in the range of pH >5 to obtain a more precise value of K_2'.

The rate of decomposition of the intermediate in solutions of pH >5 is given by equation (10), but as $k_2 = 0$, this simplifies to:

$$k = k_1/(1 + K_2' f_i^-/a_{H^+} f_i^=) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10b)$$

i.e., $\log K_2' - \log a_{H^+} + \log f_i^-/f_i^= = \log(k_1/k - 1)$. Plotting pH + $\log f_i^-/f_i^=$ against $\log(k_1/k - 1)$ gives a straight line, as shown by data in Table 4, and a value for the second ionisation constant of the intermediate $K_2' = 1{\cdot}12 \times 10^{-7}$ mole l.$^{-1}$. The straight line obeys the equation

$$\log(k_1/k - 1) = 1{\cdot}06\{\text{pH} + \log(f^-/f^=) - 6{\cdot}95\}$$

The experimentally observed slope is 1·06, whereas equation 10(*b*) predicts that it should be unity. This discrepancy is presumably due to the approximations made in assigning numerical values to the hydrogen-ion activity and the activity coefficients.

TABLE 4.

			log $(k_1/k - 1)$					log $(k_1/k - 1)$	
pH	I	pH + log $(f^-/f^=)$	Obs.	Calc.	pH	I	pH + log $(f^-/f^=)$	Obs.	Calc.
6·23	0·065	6·53	−0·41	−0·46	7·30	0·123	7·68	0·75	0·77
6·76	0·090	7·11	0·17	0·16	7·68	0·120	8·06	1·20	1·19
7·01	0·030	7·23	0·25	0·30	9·19	0·130	9·57	2·82	2·78
7·01	0·129	7·40	0·47	0·49	9·58	0·130	9·96	3·18	3·19

The values of K, observed in the pH range 5—9, are compared in Table 5 with those calculated from equation (7), both the potentiometrically determined value for $\bar{K}_2$ (Crouthamel *et al.*, *loc. cit.*) and that determined in this work by pH measurements in periodic acid buffer being used.

TABLE 5.

		K (l. mole^{-1})					K (l. mole^{-1})		
pH	I	Obs.	Calc.[1]	Calc.[2]	pH	I	Obs.	Calc.[1]	Calc.[2]
5·25	0·050	188	196	194	7·01	0·129	540	556	359
6·23	0·065	237	250	229	7·68	0·120	1000	1130	469
6·76	0·090	345	400	305	9·58	0·130	~2500	1820	529
7·01	0·030	476	455	325					

[1] Taking $\bar{K}_2 = 1{\cdot}16 \times 10^{-8}$ (this work). [2] Taking $\bar{K}_2 = 4{\cdot}0 \times 10^{-8}$ (Crouthamel *et al.*, *loc. cit.*).

The values obtained in this work for the various equilibrium and rate coefficients are given in Table 6, together with the values of earlier workers.

TABLE 6. *Rate and equilibrium coefficients.*

Coeff.	Value	Method of determination
K_1	$3{\cdot}6 \times 10^{-3}$	From plot of K (pH ~2)
	4×10^{-3}	Spectrophotometric (Crouthamel *et al.*, *loc. cit.*)
	$4{\cdot}0 \times 10^{-3}$	Buffer measurements
K_2	$4{\cdot}0 \times 10^{-8}$	Potentiometric (as above)
	$1{\cdot}16 \times 10^{-8}$	Buffer measurements
K_1'	$7{\cdot}4 \times 10^{-2}$	From $1/k$ plot (pH 1—4)
	$6{\cdot}8 \times 10^{-2}$	From K plot (pH ~2)
K_2'	$1{\cdot}12 \times 10^{-7}$	From log $[k_1/k - 1]$ plot (pH 6—9)
	$1{\cdot}16 \times 10^{-7}$	From $1/k$ plot (pH 4—7)
k_1	$45{\cdot}7 \times 10^{-4}$	From $1/k$ plot (pH 1—4)
	$45{\cdot}7 \times 10^{-4}$	From $1/k$ plot (pH 5—7)
K'	189	From results at pH 4·3

DISCUSSION OF RESULTS

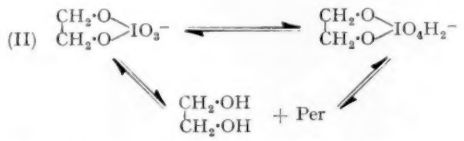
All the experimental results on the kinetics of oxidation of ethylene glycol by periodic acid can be explained in terms of the singly-negatively charged intermediate as the sole decomposing species.

In the quantitative consideration of the effect of acidity on reaction rate we consider salt effects simply as the effect of ionic strength on the equilibria involved, and the results obtained suggest that salt effects on the rate coefficient, k_1, can be neglected.

It is relevant to speculate on the reason for the singly-negatively charged intermediate's being the sole decomposing entity. As was pointed out, the effects of acidity and ionic strength give no differentiation between the hydrated and the dehydrated intermediate species. We suggest that the decomposing entities must be the dehydrated species, and such dehydration cannot occur with the doubly negatively charged intermediate (IV), which is therefore not a decomposing entity.

The decomposition of the dehydrated uncharged intermediate formed by the change (V) $\rightleftharpoons$ (VI) + H_2O may be considered a possibility, but the molecule (VI) would be a strong acid, and would be fully ionised under all our experimental conditions. We have been unable, for ethylene glycol, to extend our measurements to solutions of acidity high enough to observe the existence of this neutral intermediate species.

We therefore consider the decomposition of the singly negatively charged intermediate formed by



The decomposition of (II) would be a reaction involving no formation or destruction of charge, and so would not be subject to a large salt effect, and it would show the general characteristics of an internal rearrangement:

It would therefore be idle to speculate on the nature of the carbon–carbon bond fission for this decomposition (Hughes and Ingold, *Quart. Reviews*, 1952, **6**, 34).

EXPERIMENTAL

Materials.—Ethylene glycol (B.D.H.) was distilled before use. Sodium metaperiodate was prepared from the paraperiodate (Hill, *J. Amer. Chem. Soc.*, 1928, **50**, 2679) and recrystallised from water. Potassium dimesoperiodate ($K_4I_2O_9,9H_2O$) was prepared from potassium metaperiodate and potassium hydroxide and recrystallised from water.

The following buffer solutions were used: pH 3—5, sodium acetate–perchloric acid;

pH 5—7·5, sodium dihydrogen phosphate–sodium hydroxide; pH 8·5—10, ammonia—perchloric acid.

Below pH 3 a buffer is unnecessary, as the pH change in the course of the reaction has a negligible effect on rate, and here the pH was adjusted by the addition of perchloric acid.

Sodium perchlorate (recrystallised) was used to adjust the ionic strength where necessary.

Kinetic Measurements.—All kinetic measurements were carried out in aqueous solution at 0°, with 0·001M-periodate solutions. Measurements at a given pH and ionic strength were independent of the buffer and the source of the periodate.

At arbitrary times aliquot parts of the reaction mixture were quenched in potassium iodide. As the reaction between potassium iodide and periodate is slow in neutral solution, the usual method for the determination of periodate (Jackson, "Organic Reactions," Vol. II, p. 361, Wiley, 1944) was slightly modified. A mixture of 2 c.c. of 4M-potassium iodide and 5 c.c. of 1M-sodium hydrogen carbonate solution was added to 10-c.c. portions of the reaction mixture. The samples, after standing, at 0° to prevent loss of iodine, were titrated with 0·0005M-sodium arsenite, with a starch indicator. Total glycol concentration was determined by addition of excess of periodate.

pH *Measurements.*—pH's were measured with a Cambridge pH meter, a glass electrode being used. A silver–silver chloride reference electrode was used with a conventional ground-glass cap liquid junction. The meter was standardized with a 0·05M-phthalate buffer, pH 4·00 at 0°.

Examples of two kinetic runs are given below:

Run No. 93. pH = 0·95, I = 0·134, $[\text{Glycol}]_\infty$ = 0·093M, $[\text{Periodate}]_0$ = 0·00087M.

Time (sec.)	0	120	240	360	480	600	720	840	960
Titre (obs.), c.c.	7·99	6·88	5·91	5·14	4·39	3·74	3·21	2·83	2·35
Titre (calc.), c.c. ...	7·99	6·88	5·90	5·08	4·36	3·74	3·22	2·77	2·38

Calculated titre = $7{\cdot}99e^{-k't}$; k' = 12·62 × 10^{-4} sec.$^{-1}$.

Run No. 103. pH = 4·34, I = 0·134, $[\text{Glycol}]_\infty$ = 0·0214M, $[\text{Periodate}]_0$ = 0·00091M.

Time (sec.)	0	55	106	160	215	275	325	375	420
Titre (obs.), c.c.	9·09	7·48	6·20	5·10	4·20	3·31	2·78	2·31	1·91
Titre (calc.), c.c. ...	9·09	7·45	6·17	5·07	4·14	3·33	2·77	2·31	1·95

Calculated titre = $9{\cdot}09e^{-k't}$; k' = 36·6 × 10^{-4} sec.$^{-1}$.

Runs with periodate in excess gave results identical with those with glycol in excess.

In all cases the values of k and K, the rate and equilibrium coefficients for the formation and decomposition of the intermediate, were obtained by plotting $1/k'$ against 1/[Glycol] (Fig. 1). Slight deviations from a straight line are noticed at high glycol concentrations. Such deviations were noticed previously by Duke and Bremer (*Iowa State Coll. J. Sci.*, 1951, **25**, 527; *Chem. Abs.*, 1951, **45**, 8390); they may be due to the formation of diglycol intermediate species, as pointed out by the above workers, but in general the deviations become marked only when the glycol is in sufficiently high concentration to change the solvent properties of the medium.

Apparent Ionisation Constants of Periodic Acid.—The first and the second apparent ionisation constants of periodic acid were determined by measuring the pH of periodate buffers in aqueous solution at 0°. For the determination of $\bar{K}_1$, a 0·08M-solution of sodium metaperiodate was mixed with the half-equivalent amount of perchloric acid. For $\bar{K}_2$, the buffer was made up similarly with 0·005M-potassium dimesoperiodate, and a half-equivalent of sulphuric acid added. Carbonate-free solutions were used.

Activity coefficients were calculated as previously described.

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William Ramsay & Ralph Forster Laboratories,
University College, Gower St., London, W.C.1. [*Received, December 8th*, 1953.]

1 : 2 : 3 : 4-*Tetrahydro*-6-*hydroxy*-7-*methylcarbazole and* 3-*Hydroxy*-2-*methylcarbazole.*

By José A. Cummins, B. F. Kaye, and Muriel L. Tomlinson.

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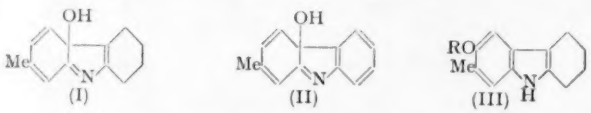
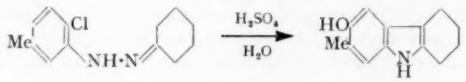
1 : 2 : 3 : 4-Tetrahydro-6-hydroxy-7-methylcarbazole and 3-hydroxy-2-methylcarbazole have been synthesised and have been shown to be identical with a substance, $C_{13}H_{15}ON$ (isolated as a by-product in the preparation of 8-chloro-1 : 2 : 3 : 4-tetrahydro-5-methylcarbazole from *cyclo*hexanone 6-chloro-*m*-tolylhydrazone)*, and its dehydrogenation product, $C_{13}H_{11}ON$, respectively.

It was shown (Milne and Tomlinson, *J.*, 1952, 2789) that the so-called "12-hydroxy-1 : 2 : 3 : 4-tetrahydro*iso*carbazole" and "12-hydroxy*iso*carbazole" described by Barnes, Pausacker, and Schubert (*J.*, 1949, 1381) are actually 1 : 2 : 3 : 4-tetrahydro-6-hydroxycarbazole and 3-hydroxycarbazole, respectively. Earlier Pausacker and Robinson (*J.*, 1947, 1557) had very tentatively suggested the *iso*carbazole structures (I) and (II) for a by-product, $C_{13}H_{15}ON$, obtained while carrying out the Fischer reaction with *cyclo*hexanone 6-chloro-*m*-tolylhydrazone, and its dehydrogenation product, $C_{13}H_{11}ON$, because these compounds were apparently devoid of phenolic character. It has now been proved, as could be expected from Milne and Tomlinson's observations, that these two substances



are, nevertheless, 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-7-methylcarbazole (III; R = H) and 3-hydroxy-2-methylcarbazole, respectively, by comparison of them with authentic specimens.

The compound (III; R = Me) was prepared by the Fischer reaction from 4-methoxy-*m*-tolylhydrazine and *cyclo*hexanone: only one product was isolated. It is assumed that this must be the 7- and not the 5-methyl derivative from its identity with the methoxy-derivative of the by-product from the cyclisation of *cyclo*hexanone 4-chloro-*m*-tolylhydrazone. This by-product must have arisen by ring-closure with the elimination of the



chlorine atom, the main product of the reaction being, of course, 8-chloro-1 : 2 : 3 : 4-tetrahydro-5-methylcarbazole. Demethylation of (III; R = Me) afforded authentic 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-7-methylcarbazole (III; R = H) and dehydrogenation and demethylation of (III; R = Me) gave 3-hydroxy-2-methylcarbazole.

Experimental

1 : 2 : 3 : 4-*Tetrahydro*-6-*hydroxy*-7-*methylcarbazole.*—(*a*) 4-Methoxy-*m*-toluidine * (4·7 g.) in hydrochloric acid (9 c.c.) and water (12 c.c.) was diazotised between −5° and 0° with sodium nitrite (2·5 g. in a little water). The violet diazonium salt solution was filtered through glass-wool into stannous chloride (18 g.) and hydrochloric acid (24 c.c.) at −10° to −5°. The hydrazine salt thus formed was collected after being kept at 0° for 1 hr. and then for 12 hr. at room temperature. After being washed with cold brine it was suspended in water and treated with *cyclo*hexanone (3·6 g.) and excess of sodium acetate. The crude hydrazone, which

* In these substituted toluenes, the group named as a suffix or, in the case of the tolyl radical, the free valency is numbered 1.

separated as a red paste, was collected, washed with water, and dissolved in alcohol and the solution filtered to remove inorganic matter. After precipitation with water the hydrazone was directly converted into 1 : 2 : 3 : 4-*tetrahydro-6-methoxy-7-methylcarbazole* by boiling it with sulphuric acid (2N; 75 c.c.). The product crystallised from alcohol as needles, m. p. 172° (Found : C, 78·4; H, 7·9. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9%). This compound (0·5 g.) was boiled with acetic acid (5 c.c.) and hydrobromic acid (50%; 1 c.c.) in an atmosphere of carbon dioxide for 2 hr. After the solution had cooled, water precipitated 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-7-methylcarbazole which crystallised from benzene as plates, m. p. 208° (brown liquid and some softening at 200°).

This compound is practically insoluble in 2N-sodium hydroxide, although the mixture of the two darkens when kept; addition of a drop of aqueous ferric chloride to its alcoholic solution gives a brownish-violet colour. (*b*) The substance $C_{13}H_{15}ON$ was prepared as described by Pausacker and Robinson (*loc. cit.*); it was recrystallised from benzene and was now obtained as colourless plates, m. p. 208° (brown liquid and softening at 200°) unaltered on admixture with 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-7-methylcarbazole prepared as under (*a*) above (Found : C, 77·4; H, 7·5. Calc. for $C_{13}H_{15}ON$: C, 77·6; H, 7·5%). It (1·2 g.) was mixed with acetone (10 c.c.) and potassium hydroxide (0·7 g. in a little water) and treated gradually with methyl sulphate (1·5 g.). Addition of water precipitated 1 : 2 : 3 : 4-tetrahydro-6-methoxy-7-methylcarbazole which crystallised from alcohol as needles, m. p. 169° raised to 170° by admixture with that compound prepared as under (*a*).

3-*Methoxy-2-methylcarbazole.*—(*a*) 1 : 2 : 3 : 4-Tetrahydro-6-methoxy-7-methylcarbazole (0·5 g.) was heated with palladised charcoal (0·15 g.; containing 10% of palladium on norite) at 200—220° in a stream of carbon dioxide for 2 hr. The product was extracted with acetone, precipitated with water, and collected. Recrystallisation from alcohol afforded 3-*methoxy-2-methylcarbazole* as needles, m. p. 179—181·5°. (*b*) Similar dehydrogenation of the tetrahydro-methoxymethylcarbazole prepared as described under (*b*) above afforded 3-methoxy-2-methylcarbazole, m. p. 179—181·5° unaffected by admixture with that compound prepared from the synthesised tetrahydro-compound (Found : C, 79·9; H, 6·3. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2%).

3-*Hydroxy-2-methylcarbazole.*—(*a*) 3-Methoxy-2-methylcarbazole (0·45 g.; synthetic) was boiled with acetic acid (5 c.c.) and hydrobromic acid (50%; 1 c.c.) with frequent shaking during 1 hr. and then a further equal quantity of acetic and hydrobromic acids was added. Refluxing was continued for another hour. On cooling, the product crystallised, was collected, and recrystallised from benzene, from which 3-hydroxy-2-methylcarbazole separated as needles which began to darken about 270° and finally melted to a black liquid at 316°. It was practically insoluble in 2N-sodium hydroxide though the mixture darkened when kept; a green precipitate was formed when a drop of aqueous ferric chloride was added to its alcoholic solution. (*b*) The by-product, $C_{13}H_{15}ON$, from the Fischer reaction with *cyclo*hexanone 6-chloro-*m*-tolylhydrazone was dehydrogenated as above at 280—300°, and the product, after extraction with acetone and precipitation with water, was recrystallised from benzene. It separated as needles that softened at 260°, darkened, and finally melted to a black liquid at 316° (Found : C, 79·1; H, 5·7. Calc. for $C_{13}H_{11}ON$: C, 79·2; H, 5·6%). The m. p. was previously found to be 262° (decomp.). Comparison of the infra-red spectra of specimens made as described under (*a*) and (*b*) showed that the two are identical.

4-*Amino-o-cresol.*—This substance (used as an intermediate in the preparation of 4-methoxy-*m*-toluidine) has previously been prepared by reduction of 4-nitroso-*o*-cresol with ammonia and hydrogen sulphide (Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 3198) but the following is more convenient. Crude 4-nitroso-*o*-cresol, from *o*-cresol (30 g.) (Bridge and Morgan, *Amer. Chem. J.*, 1898, **20**, 766), was dissolved in cold sodium carbonate solution (2N) and filtered to remove unchanged cresol. To this was then added gradually, with stirring, sodium dithionite (50 g.). The amine (16 g.; m. p. 170—173°) separated and was collected.

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THE DYSON PERRINS LABORATORY, OXFORD. [*Received, January 9th*, 1954.]

*Vapour-phase Oxidation of Olefins. The Catalysed Oxidation of Diisobutene in the Presence of Selenium.**

By D. J. Hadley, R. H. Hall, R. Heap, and D. I. H. Jacobs.

[Reprint Order No. 4840.]

The oxidation of di*iso*butene [equilibrium mixture of 2 : 4 : 4-trimethylpent-1- and -2-ene, (I) and (II), respectively] with air or oxygen in the vapour phase over a supported copper catalyst at 250—350° in the presence of selenium gave a mixture of 4 : 4-dimethyl-2-methylenepentanal (III) (α-*neo*pentylacraldehyde) and 2 : 4 : 4-trimethylpent-2-enal (IV) as major product. Similar oxidations of (I) containing a little (II), and (II) containing a little (I), indicated that (III) arose mainly from (I), and (IV) mainly from (II).

The methyl ester of 4 : 4-dimethyl-2-methylenepentanoic acid,† derived from (III), could not be polymerised by heating it with benzoyl peroxide under standard conditions.

The problem of the partial oxidation of olefins in the vapour phase has attracted many investigators. Success depends largely on the use of a selective catalyst which will promote formation of desirable products without causing scission of carbon–carbon bonds and subsequent formation of large proportions of carbon oxides. Metallic silver (suitably supported), which enables good yields of ethylene oxide to be obtained from ethylene,[1] is a typical example of such a catalyst.

Clark and Shutt (U.S.P. 2,383,711) passed propene and other olefins with air over a metallic selenite or tellurite, preferably silver selenite, at 270—320°, and obtained reasonable yields of unsaturated carbonyl compounds containing the same number of carbon atoms per molecule as the corresponding olefins. The addition of metallic oxides, such as cupric oxide, to the silver selenite was recommended but the catalyst, with or without cupric oxide, rapidly lost its activity. Hadley and his co-workers (B.P. 625,330, 648,386, 655,210, 658,179, 658,240) developed an efficient catalyst which consisted essentially of copper and selenium. Since selenium is volatile at the temperatures employed there was need for a continuous transport of it over the copper and it was found best to use the copper in the form of copper aluminate or copper silicate. The present paper describes the application of the oxidation method to di*iso*butene.

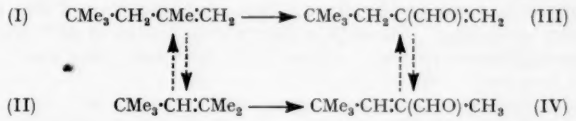
In preliminary experiments with this olefin the catalyst was copper aluminate (for preparation, see Hadley, Heap, and Nichol, B.P. 655,210; example 1 of complete specification); it was then found that copper silicate was a more efficient catalyst, and all subsequent work was carried out with this.

Passage of di*iso*butene [equilibrium mixture of (I) and (II)], admixed with air and selenium vapour, over the catalyst at 250—350° gave as main product a mixture of C_8 mono-olefinic aldehydes which was shown to consist of 4 : 4-dimethyl-2-methylenepentanal (III) (α-*neo*pentylacraldehyde), b. p. 147—148°, and 2 : 4 : 4-trimethylpent-2-enal (IV), b. p. 162—163°, in the proportions of 3 to 1 approx. When (I) containing 3—4% of (II) was employed in place of the equilibrium mixture of isomers, (III) was the major (78%) constituent of the C_8 aldehyde fraction; (IV) pre-dominated (61%) when (II) containing 5% of (I) was oxidised. The structures of the aldehydes were established by methods described below.

The ready isomerisation of (I) and (II) in the presence of catalysts to give the equilibrium mixture of the isomers is well known [cf. the work of Gallaway and Murray, *J. Amer. Chem. Soc.*, 1948, **70**, 2584, on the isomerisation of (I) and (II) over silica gel at room temperature]. In the present work it was shown that passage of (I) over activated alumina at 275° in the absence of air or oxygen resulted in partial isomerisation to (II); the process was not studied with (II) owing to the limited supplies. Hence the formation of both (III) and (IV) during the oxidation of either (I) or (II) might have been due to partial

* This work is the subject of B.P. 694,353 and 694,362. † Geneva nomenclature, $CO_2H = 1$.

isomerisation of the pure olefins, followed by oxidation. The latter must have occurred more readily than the isomerisation, for different proportions of (III) and (IV) were obtained depending on the proportions of (I) and (II) in the starting material. It is also conceivable (although no direct evidence was obtained) that the C_8 aldehydes themselves isomerised to some extent over the catalyst, since this could be slowly effected (concurrently with polymerisation or association) by refluxing the liquids at atmospheric pressure.



Small amounts of α-methylacraldehyde were isolated from all the oxidations and probably arose from the *iso*butene formed by thermal fission of the di*iso*butene. The other main by-products were carbon dioxide and materials of high molecular weight. The amount of the latter varied with the severity of heating of the crude product during fractionation and was reduced by distillation in steam or under reduced pressure. Small amounts of the C_8 aldehydes were produced by thermal decomposition of these compounds of high molecular weight, for example, during distillation.

In the above preliminary experiments difficulty was experienced in condensing the C_8 aldehydes completely in cold traps, either because they formed aerosols or because the exit gases were readily supersaturated with them. As an increase of contact time over the catalyst beyond the optimum caused little further oxidation of the C_8 aldehydes a re-cycle system was tried (see p. 1419) : the main feature of this was that part of the gas leaving the reaction vessel was fed back to the entrance of this vessel after being replenished with oxygen, di*iso*butene, and selenium. By re-cycling, the concentration of product in the gas leaving the apparatus was increased and the loss due to incomplete condensation was reduced.

The structures of the aldehydes (III) and (IV) were established in the following way. Elementary analyses and ultra-violet absorption properties of the substances and their derivatives demonstrated that they were αβ-unsaturated C_8 carbonyl compounds. Hydrogenation of each gave, first, the known 2 : 4 : 4-trimethylpentanal and then 2 : 4 : 4-trimethylpentan-1-ol, and oxidation with silver oxide in alkaline media or, in one case, with molecular oxygen, gave the corresponding unsaturated C_8 carboxylic acids which on hydrogenation furnished the same saturated acid, 2 : 4 : 4-trimethylpentanoic acid. From these facts it followed that the aldehydes possessed the isomeric structures (III) and (IV). Assignment of (III) to the aldehyde of b. p. 147—148° and of (IV) to that of b. p. 162—163° was indicated by infra-red studies and proved by ozonolysis : the higher-boiling compound gave the expected trimethylacetaldehyde and methylglyoxal, whereas the isomer gave formaldehyde, *tert.*-butylacetic acid, and traces of glyoxal. The formation of *tert.*-butylacetic acid is in accord with the fact that Whitmore and Church (*J. Amer. Chem. Soc.*, 1932, **54**, 3710) obtained this acid in small amounts from the ozonolysis of the corresponding isomer of di*iso*butene, namely, (I). It presumably arose in both cases by a similar mode of decomposition of the intermediate ozonide. However, the production of formaldehyde in high yield from (III) is evidence that the latter contains a methylene group, although it is possible that not all of the formaldehyde obtained arose from this group.

Although (III) and (IV) were both new compounds when first prepared by us, (III) has recently been described by Smith, Norton, and Ballard (*ibid.*, 1951, **73**, 5284) who stated that it was made by Hearne and Adams (U.S.P. 2,486,842). No details of (III) were given, however, in this patent specification.

The unsaturated acids derived from (III) and (IV) were clearly 4 : 4-dimethyl-2-methylenepentanoic acid and 2 : 4 : 4-trimethylpent-2-enoic acid, respectively. The methyl ester of the former, prepared *via* the acid chloride, could not be induced to polymerise on being heated with benzoyl peroxide; the bulky α-*neo*pentyl grouping presumably exerted a strong steric hindrance.

Experimental

Preparation of Copper Silicate Catalyst.—A solution of commercial sodium metasilicate (1 part, containing about 50% w/w of Na_2SiO_3) in water (20 parts) was added during 2 min. to a vigorously stirred solution of cupric nitrate trihydrate (2 parts) in cold water (about 10 parts). The resulting light blue precipitate was collected on a Buchner funnel and sucked as dry as possible. The filter cake was dried at 80—100°, heated in a stream of air at about 300° in order to decompose any excess of copper nitrate, and then formed into cylindrical pellets, $\frac{1}{8}$ in. in diameter by $\frac{1}{16}$ in. long. Finally the pellets were heated at 600° for $1\frac{1}{2}$ hr. The final heat treatment and the avoidance of washing of the filter cake were essential for an efficient catalyst.

Oxidation of Diisobutene.—Preliminary experiments were carried out in the helical glass tubing reaction vessel shown in Fig. 1. The di*iso*butene was introduced into the air stream by allowing the air to bubble through liquid di*iso*butene in a vessel kept in a water-bath maintained at 15° ± 0·5°, while the selenium vapour was introduced by suspending a small cup (*A*)

Fig. 1.

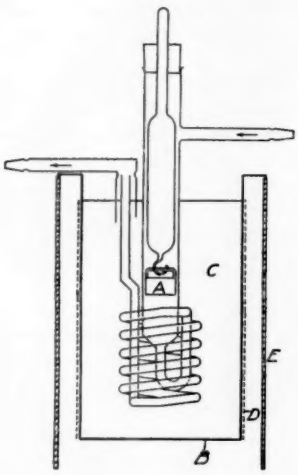
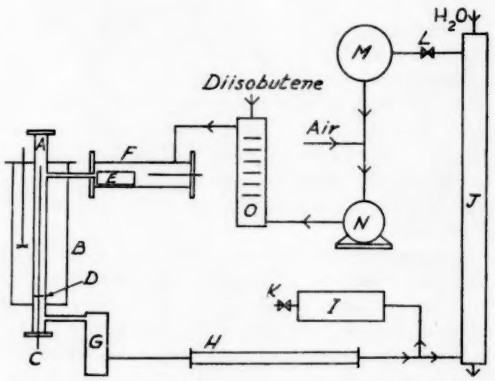


Fig. 2.



containing molten selenium in the entrance chamber of the reaction vessel. The reaction vessel, including the larger part of the entrance chamber, was immersed in a heating bath (*B*) containing a molten mixture (*C*) of sodium nitrite and potassium nitrate electrically heated by the winding (*D*) and lagged by a cylinder (*E*) of asbestos–cement and thermostatically kept at a temperature of 320° ± 2°.

The products of the reaction were collected in three traps in series, the first at room temperature, the second cooled in solid carbon dioxide–acetone, and the third in liquid air. At the end of a run, the contents of the traps were mixed and steam-distilled, and the upper layer in the distillate was separated and fractionated at atmospheric pressure through a column (40 cm. long, 1·5 cm. diam.) packed with single-turn glass helices. Samples of gas taken after the first trap were analysed for carbon dioxide in a Bone and Wheeler apparatus. An aliquot portion of the aqueous layer of the steam-distillate was titrated with hydroxylamine reagent for carbonyl content.

In a typical run, air (20 l. at room temperature and pressure), di*iso*butene (1·65 g., equilibrium mixture of isomers), and selenium vapour (0·025 g.) were passed per hour over the copper silicate catalyst (16 g.) at 320° for 56 hr. After exhaustive steam-distillation of the combined products and separation of the two layers in the steam-distillate an upper (oil) layer of 77·8 g. was obtained. The aqueous layer contained carbonyl compounds equivalent to 6·4 g. of α-methylacraldehyde. Some resinous material (5 g. approx.) was not steam-volatile.

Distillation of the upper layer afforded fractions : (i) b. p. 60—90° (6·2 g.); (ii) b. p. 90—110° (23·5 g.); (iii) b. p. 110—140° (4·3 g.); (iv) b. p. 140—165° (31·9 g.); and residue (10 g.).

Re-fractionation of (i) gave α-methylacraldehyde (odour), b. p. 65—75°, which rapidly polymerised in the absence of inhibitor, and (ii) was mainly unchanged di*iso*butene containing a little α-methylacraldehyde. Re-fractionation of the main bulk of (iv) gave first pure α-*neo*pentylacraldehyde (III) (4 : 4-dimethyl-2-methylenepentanal) as a pale yellow liquid, b. p. 147—148°, n_D^{20} 1·4363 (Found: C, 76·35; H, 11·15. Calc. for $C_8H_{14}O$: C, 76·15; H, 11·2%); ultra-violet absorption max. in EtOH: 2240 and 3150 Å (ε 6000 and 36, respectively). (Smith *et al.*, *loc. cit.*, gave b. p. 149—150°, n_D^{20} 1·4363, d_4^{20} 0·840.) This was followed by 2 : 4 : 4-*trimethylpent-2-enal* (IV), b. p. 162—163°, n_D^{20} 1·4527 (Found: C, 76·0; H, 11·15. $C_8H_{14}O$ requires C, 76·15; H, 11·2%); ultra-violet absorption max. in EtOH: 2300 and 3080 Å (ε 11000 and 43, respectively). The proportions of (III) and (IV) were 3 to 1 approx.

The α-*neo*pentylacraldehyde readily gave a 2 : 4-*dinitrophenylhydrazone*, which crystallised from 95% ethanol as red prisms, m. p. 163° (Found: C, 54·95; H, 5·85. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9%); ultra-violet absorption max. in EtOH: 3720 Å (ε 2·1 × 10^4), and a *semicarbazone*, which separated from aqueous alcohol as white crystals, m. p. between 202° and 209° (depending on the rate of heating) (Found: C, 58·65; H, 9·2; N, 22·9. $C_9H_{17}ON_3$ requires C, 58·95; H, 9·35; N, 22·9%).

The 2 : 4 : 4-trimethylpent-2-enal readily gave a 2 : 4-*dinitrophenylhydrazone*, which separated from ethyl acetate–ethanol in long, thin, red rods, m. p. 203—204° (Found: C, 55·15; H, 5·8; N, 18·3. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%), light absorption max. in EtOH: 3780 Å (ε 2·7 × 10^4), and a *semicarbazone*, which separated from aqueous ethanol in long flattened needles, m. p. 170—171° (Found: C, 59·45; H, 9·35; N, 23·0. $C_9H_{17}ON_3$ requires C, 58·95; H, 9·35; N, 22·9%).

Analysis of the original fractions (i)–(iv) from the distillation of the oil layer of the steam-distillate (see above) showed that they contained the following (total quantities): (*a*) unchanged di*iso*butene (25·4 g.); (*b*) C_8 mono-olefinic aldehydes (34·0 g.); and (*c*) α-methylacraldehyde (6·5 g.) (a further 6·4 g. were present in the aqueous layer of the steam-distillate). The yields, based on an input of 93 g. of di*iso*butene, were thus: di*iso*butene recovered, 28%; α-methylacraldehyde, 11%; C_8 mono-olefinic aldehydes, 32·5%; high-boiling residues, 12—15% (calc. as C_8 aldehyde). The exit gases contained 3·7% of carbon dioxide, equivalent to a yield of 7%. Fraction (iv), on analysis by infra-red spectroscopy, was shown to contain 68% of α-*neo*pentylacraldehyde and 23% of 2 : 4 : 4-trimethylpent-2-enal.

Other mixtures of the two isomers were similarly oxidised. In each case the fraction of the product boiling between 140° and 165° was analysed by infra-red spectroscopy. The results are summarised in the Table.

The impurities present in the 140—165° fractions analysed by infra-red spectroscopy were not identified.

Variation of isomeric composition of C_8 *aldehyde with variation of isomeric composition of feedstock.*

Composition of feedstock, %		Composition of C_8 aldehyde, %	
Trimethylpent-1-ene	Trimethylpent-2-ene	α-*neo*Pentylacraldehyde	2 : 4 : 4-Trimethylpent-2-enal
96—97	3—4	78	18
80	20	68	23
5	95	17	61

Partial Isomerisation of 2 : 4 : 4-*Trimethylpent*-1-*ene*.—Nitrogen (20 l./hr.) was saturated at 15° with 2 : 4 : 4-trimethylpent-1-ene (1·65 g./hr.; 95% purity) and then passed through the standard glass helical reaction vessel (see above) which contained activated alumina (20 g., 8—18 mesh) and was kept at 275°. The effluent gases were passed through a trap cooled in solid carbon dioxide–acetone. After 24 hr. the condensate was removed and distilled without fractionation, and the distillate analysed by infra-red spectroscopy. It contained 70% of trimethylpent-1-ene and 30% of trimethylpent-2-ene.

Oxidation of Diisobutene in a Re-cycle Apparatus.—Fig. 2 is a diagram of the apparatus. The reaction vessel (*A*) was a vertical, ¾-inch bore, stainless-steel tube, which protruded through the bottom of a 5-in. diameter bath (*B*) of the same material. The liquid in the bath, which was about 30 in. deep, contained the same mixture as that described for Fig. 1; it was heated electrically by a winding on the outside of the container and thermostatically controlled. Vigorous stirring ensured a uniform temperature. A thermocouple pocket (*C*) carried, at a point 3 in. from the bottom of the bath, a grid (*D*), which supported the catalyst. Gas entered the top of the reaction vessel after passing over molten selenium contained in a tray (*E*) having a horizontal, rectangular, cross-section of 1 × 6 in. The selenium tray was placed in an

electrically heated chamber (*F*) thermostatically controlled at 300°, and the selenium transport was adjusted by altering the area of tray covered by a sliding lid. Gas leaving the reaction vessel passed downwards through a metal vessel (*G*) of 12 sq. in. cross section and 12 in. in height in which selenium (together with some selenium dioxide and unidentified resinous material) condensed. The gas issued from the selenium collector at about 100° and then passed through an air-cooled condenser (*H*) at the end of which part of the gas stream was vented *via* a trap (*I*), cooled in a solution of solid carbon dioxide in alcohol, while the remainder passed up a packed tower (*J*) down which a stream of water flowed. The liquid condensing in (*H*) ran down into the base of (*J*). The proportioning of flow between main stream and vent was effected by means of valves *K* and *L*. On emerging from the top of the tower, the recycled gas passed through a gas meter (*M*) and a pump (*N*) into the di*iso*butene evaporator (*O*) which contained a series of filter-papers spaced vertically, at intervals, on to which di*iso*butene was dripped at a measured rate. Subsequently the gas entered the selenium evaporator. At the end of a run the liquid effluent from (*J*) and the condensate in (*I*) were combined, and the products recovered by steam-distillation.

In a typical run with 2 : 4 : 4-trimethylpent-1-ene (96% purity, the other 4% being the 2-ene isomer) the following conditions were employed : ratio of re-cycle gas to make-up gas, 4 to 1; temp. of bath, 320°; max. temp. in catalyst bed, 334°; vol. of gas entering reactor, 400 l. per hr.; concn. of olefin in gas entering reactor, 2·1% v/v; wt. of selenium evaporated, 0·39 g. per hr.; weight of copper silicate catalyst, 170 g. (130 ml.); duration of run, 25 hr. The yields calculated on olefin fed to the system were : C_8 aldehydes, 36%; α-methylacraldehyde, 2%; carbon dioxide, 6%. The efficiency of conversion of olefin into C_8 aldehyde was 64%, and 12% of the olefin fed was unaccounted for.

The products from several oxidations similar to the above were combined and distilled through a 100-plate column, to give α-*neo*pentylacraldehyde, b. p. 147—148° (92% of total C_8 aldehyde) and 2 : 4 : 4-trimethylpent-2-enal, b. p. 162—163° (8%).

Hydrogenation of α-neo*Pentylacraldehyde to* 2 : 4 : 4-*Trimethylpentanal*.—A solution of α-*neo*pentylacraldehyde (6·9 g.) in ethanol (35 c.c.) was shaken with Raney nickel (2 g. of " paste ") to remove traces of selenium, the mixture filtered, and the catalyst washed with a little ethanol. The combined filtrate and washings were hydrogenated at atmospheric pressure and temperature over fresh Raney nickel (2 g. of " paste ") until slightly more than 1 mol. of hydrogen had been absorbed. Interruption of the reaction, filtration, and isolation of the product by fractional distillation afforded 2 : 4 : 4-trimethylpentanal (2·0 g.), b. p. 39°/9 mm., n_D^{20} 1·4155 (Hickinbottom, *J.*, 1948, 1331, gives b. p. 149—151°, n_D^{20} 1·4180), which readily gave a 2 : 4-dinitrophenylhydrazone, bright yellow needles, m. p. 145°, from ethanol (Byers and Hickinbottom, *ibid.*, p. 1328, give m. p. 143—144°), and a semicarbazone, m. p. 115°, from aqueous ethanol (Hickinbottom, *loc. cit.*, gives m. p. 118—120°).

Hydrogenation of α-neo*Pentylacraldehyde to* 2 : 4 : 4-*Trimethylpentan*-1-*ol*.—A solution of α-*neo*pentylacraldehyde (10 g.) in ethanol (50 c.c.) which had been pre-treated with Raney nickel (2 g. of " paste ") as described above was hydrogenated at room pressure and temperature over fresh Raney nickel (2 g. of " paste "). When the rate of hydrogenation became slow the temperature was raised gradually to 55° and kept thereat until absorption of hydrogen ceased. Isolation of the product afforded 2 : 4 : 4-trimethylpentan-1-ol (7·0 g.), b. p. 68—69°/12 mm., n_D^{20} 1·4260 (Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 643, give b. p. 78—80°/22 mm., n_D^{20} 1·4278—1·4285), which readily gave a 3 : 5-dinitrobenzoate, m. p. 73—74°, on recrystallisation from 95% ethanol (Whitmore *et al.*, *loc. cit.*, give m. p. 72·5—73·5°).

Oxidation of α-neo*Pentylacraldehyde to* 4 : 4-*Dimethyl*-2-*methylenepentanoic acid*.—(*A*) A solution of sodium hydroxide (6 g.) in water (300 c.c.) was added dropwise to a stirred mixture of silver oxide (from 15 g. of nitrate), α-*neo*pentylacraldehyde (5 g.), and water (50 c.c.); the resultant mixture was shaken mechanically overnight and filtered, and the solid washed with water. The combined filtrate and washings were extracted with ether, the ether extracts were discarded, and the aqueous solution was acidified strongly with sulphuric acid. The oil which separated was taken up in ether, the ethereal extract was washed with water, dried (Na_2SO_4), and evaporated. The oil (4·15 g.) obtained solidified, and on fractional distillation *in vacuo* afforded 4 : 4-*dimethyl*-2-*methylenepentanoic acid* (α-neo*pentylacrylic acid*) as a colourless oil (2·55 g.), which rapidly solidified to a crystalline solid, m. p. 39° (Found : C, 67·2; H, 9·85%; equiv., 144. $C_8H_{14}O_2$ requires C, 67·55; H, 9·9%; equiv., 142·2). The acid formed a *p-bromophenacyl* ester which separated from 90% ethanol in rosettes of needles, m. p. 56° (Found : C, 56·35; H, 5·4. $C_{16}H_{19}O_3Br$ requires C, 56·65; H, 5·65%).

(*B*) α-*neo*Pentylacraldehyde (126 g.) was stirred vigorously at 15° for 20 hr. while oxygen

was passed in at the rate of 2 l./hr. The liquid product (140 g.) was fractionated under reduced pressure to give: (i) b. p. <105°/70 mm. (48 g.); (ii) b. p. <105°/10 mm. (13 g.); (iii) b. p. 105—115°/10 mm. (50 g.); (iv) b. p. 50—100°/1 mm. (3 g.); and residue (26 g.). Fraction (i) was substantially pure α-*neo*pentylacraldehyde, and fraction (ii) was a mixture of this with 4 : 4-dimethyl-2-methylenepentanoic acid and acids of lower molecular weight. Fraction (iii) was substantially pure 4 : 4-dimethyl-2-methylenepentanoic acid, m. p. 37°. By melting, cooling, and draining the partially crystalline mass, the m. p. was raised to 44° (Found: equiv., 142·5). The infra-red absorption spectrum of the pure material was consistent with the assigned constitution.

The acid was converted by means of thionyl chloride into the acid chloride, and this on treatment with methanol in the presence of pyridine afforded *methyl* 4 : 4-*dimethyl*-2-*methylenepentanoate* (57% overall yield), b. p. 95°/70 mm., n_D^{20} 1·4303 (Found: C, 69·7; H, 10·0%; sap. equiv., 157; unsaturation, 1·02H_2. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%; sap. equiv., 156). The infra-red absorption spectrum of the pure ester was consistent with the assigned structure.

Hydrogenation of the acid (0·8 g.) in ethanol (25 c.c.) over Adams's platinum oxide catalyst (0·1 g.) at room temperature and pressure resulted in the absorption of 1·0 mol. of hydrogen. Isolation of the product afforded 2 : 4 : 4-trimethylpentanoic acid as an oil which was converted *via* the acid chloride ($SOCl_2$–benzene) into the anilide (m. p. 118—119°, from methanol–water) and the amide [needles, m. p. 123—124°, from light petroleum (b. p. 60—80°)]. Whitmore *et al.* (*J. Amer. Chem. Soc.*, 1941, **63**, 2028) give m. p. 117—118° and m. p. 123° for the anilide and amide, respectively, of 2 : 4 : 4-trimethylpentanoic acid.

Ozonolysis of α-neo*Pentylacraldehyde.*—Ozonised oxygen (containing about 4% w/v of ozone) was passed into a solution of α-*neo*pentylacraldehyde (2 g.) in redistilled methylene dichloride (50 c.c.), which was cooled in alcohol–solid carbon dioxide, until ozone appeared in the exit gas. The latter was bubbled through ice-cold water (50 c.c.; A) throughout the experiment. The methylene dichloride solution was evaporated *in vacuo* below room temperature and the bright greenish-yellow liquid remaining was dissolved in acetic acid (10 c.c.). The solution was added cautiously to a mixture of zinc dust (1·05 g.) and water (10 c.c.) which was shaken vigorously. The resultant mixture was steam-distilled until about 35 c.c. of distillate (B) had been collected. The residual liquid in the distilling flask was cooled, filtered, and set aside (C).

Liquid A above gave no precipitate with a solution of 2 : 4-dinitrophenylhydrazine in aqueous 2N-hydrochloric acid. With this reagent a test portion of liquid B gave a precipitate of formaldehyde 2 : 4-dinitrophenylhydrazone which crystallised from 95% ethanol as brownish-yellow crystals, m. p. and mixed m. p. 167°. A test portion of liquid C was heated with a solution of 2 : 4-dinitrophenylhydrazine in 6N-hydrochloric acid, and the small amount of derivative which separated was collected, washed with dilute hydrochloric acid, and recrystallised from glacial acetic acid. Red crystals, m. p. 314° (decomp.), were obtained (Found: C, 40·5; H, 2·4. Calc. for $C_{14}H_{10}O_8N_8$: C, 40·2; H, 2·4%) which gave an intense blue colour with alcoholic sodium hydroxide. The m. p. was undepressed on admixture of the crystals with authentic glyoxal bis-2 : 4-dinitrophenylhydrazone.

The main bulk of liquid C was extracted with ether, and the extract was washed with a little water, dried (Na_2SO_4), and evaporated *in vacuo* to give a colourless oil (0·95 g.) which gave no carbonyl reactions and appeared to be acidic. It was combined with a similar oil from another ozonolysis on the above scale and the mixture was fractionated to give, after removal of acetic acid, a colourless acid (0·4 g.), b. p. 170—180°, n_D^{20} 1·4081 (Found: equiv., 115. Calc. for $C_6H_{12}O_2$: equiv., 116). The acid formed a *p*-bromophenacyl ester, which crystallised from 95% ethanol as plates, m. p. 81—82°, and an amide, which crystallised from light petroleum (b. p. 100—120°) as leaflets, m. p. 132° (lit.: m. p. 132° for *tert.*-butylacetamide). The m. p. of the *p*-bromophenacyl ester was not depressed on admixture of the ester with an authentic specimen of *p*-bromophenacyl *tert.*-butylacetate.

In a subsequent experiment on a similar scale the total amount of formaldehyde formed on decomposition of the ozonide was estimated by the neutral sulphite method and amounted to 0·46 g. (theory for one CH_2 group, 0·48 g.).

Hydrogenation of 2 : 4 : 4-*Trimethylpent*-2-*enal to* 2 : 4 : 4-*Trimethylpentan*-1-*ol.*—A solution of the aldehyde (5 g.) in absolute ethanol (50 c.c.) was hydrogenated over Raney nickel "paste" (5 g.) at room temperature and pressure until no more hydrogen was absorbed. It afforded 2 : 4 : 4-trimethylpentan-1-ol (3·35 g.), b. p. 84°/25 mm., whose 3 : 5-dinitrobenzoate (from 95% ethanol), had m. p. 73—74°, undepressed on admixture with the derivative obtained above from the hydrogenation of α-*neo*pentylacraldehyde.

Hydrogenation of 2 : 4 : 4-*Trimethylpent-2-enal to* 2 : 4 : 4-*Trimethylpentanal.*—A solution of 2 : 4 : 4-trimethylpent-2-enal (1 g.) in absolute ethanol (30 c.c.) was hydrogenated at room temperature and pressure over Raney nickel " paste " (1 g.) until slightly more than one mol. of hydrogen had been absorbed, then filtered. The solution readily gave yellow needles (from ethanol) of 2 : 4 : 4-trimethylpentanal 2 : 4-dinitrophenylhydrazone, m. p. 144—145°, undepressed on admixture with the derivative obtained earlier from the hydrogenation of α-*neo*pentylacraldehyde.

Oxidation of 2 : 4 : 4-*Trimethylpent-2-enal to* 2 : 4 : 4-*Trimethylpent-2-enoic Acid.*—A solution of sodium hydroxide (12 g.) in water (600 c.c.) was added slowly to a stirred, cooled mixture of silver oxide (from 45 g. of nitrate), 95% ethanol (50 c.c.), water (50 c.c.), and 2 : 4 : 4-trimethylpent-2-enal (10 g.), and the resultant mixture was stirred overnight. The product was filtered, the solid was washed with water and ethanol, the combined filtrate and washings were concentrated *in vacuo* to *ca.* 100 c.c., extracted with ether, and the extract was discarded. The aqueous layer was acidified strongly with sulphuric acid and the oil which separated was extracted with ether. The ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated *in vacuo*, to give crystals (9·65 g.) which were then fractionally distilled in a micro-still. 2 : 4 : 4-*Trimethylpent-2-enoic acid* was obtained as a colourless oil (8·1 g.), b. p. 124·5/11·5 mm., m. p. 45—46°. Recrystallisation from light petroleum (b. p. 60—80°), cooled in solid carbon dioxide–alcohol, afforded a white microcrystalline solid, m. p. 47—48° (Found : C, 67·95; H, 10·0%; equiv., 143. $C_8H_{14}O_2$ requires C, 67·55; H, 9·9%; equiv., 142·2). The acid gave a p-*bromophenacyl* ester which separated from 90% ethanol–10% water as sheaves of thin needles, m. p. 79—80° (Found : C, 56·55; H, 5·75; Br, 23·95. $C_{16}H_{19}O_3Br$ requires C, 56·65; H, 5·65; Br, 23·55%). On hydrogenation of the acid (0·5 g.) in ethanol (10 c.c.) over Adams's catalyst (0·1 g.) at room temperature and pressure, 1·0 mol. of hydrogen was rapidly absorbed. Isolation of the product afforded 2 : 4 : 4-trimethylpentanoic acid, identified as described above.

Ozonolysis of 2 : 4 : 4-*Trimethylpent-2-enal.*—Ozonised oxygen (containing about 4% w/v of ozone) was passed through a solution of the aldehyde (2 g.) in redistilled methylene dichloride (50 c.c.) at the rate of about 30 c.c. per min. The aldehyde solution was cooled in a solid carbon dioxide–alcohol bath, and the gas leaving the solution was bubbled through ice-cold water (the resulting liquid was found to contain only traces of carbonyl compounds). When ozone appeared in the exit gas (after about 6 hr.) ozonolysis was stopped, the methylene dichloride solution was evaporated *in vacuo* below room temperature, and the bright greenish-yellow oil obtained was dissolved in acetic acid (10 c.c.). The solution was added cautiously, with shaking, to a mixture of zinc dust (1·05 g.) and water (10 c.c.) and the resultant mixture was diluted with water and distilled until about 7 c.c. of liquid had been collected. With 2 : 4-dinitrophenylhydrazine sulphate solution the distillate gave a copious precipitate of trimethylacetaldehyde 2 : 4-dinitrophenylhydrazone, needles (from ethanol–ethyl acetate), m. p. 209—210°, undepressed on admixture with an authentic specimen.

The liquid remaining in the distilling-flask was filtered and on treatment with 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid gave a precipitate of methylglyoxal bis-2 : 4-dinitrophenylhydrazone, which formed small brick-red crystals, m. p. and mixed m. p. 298—300° (decomp.), from pyridine (Found : C, 41·65; H, 3·05; N, 26·4. Calc. for $C_{15}H_{12}O_8N_8$: C, 41·65; H, 2·8; N, 25·9%), and gave an intense blue colour with alcoholic sodium hydroxide.

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THE DISTILLERS CO., LTD., RESEARCH AND DEVELOPMENT DEPARTMENT,
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The Periodate Oxidation of Methylfructoses.

By W. E. A. Mitchell and Elizabeth Percival.

[Reprint Order No. 5015.]

The extent of periodate oxidation of a number of methyl ethers of fructose has been measured by the determination of liberated formaldehyde and also by periodate uptake.

Periodate oxidation of methylated monosaccharides has been studied extensively by Bell (*J.*, 1948, 992), and Bell, Palmer, and Johns (*J.*, 1949, 1536). In the latter paper, the oxidation of 1 : 3 : 4- and 3 : 4 : 6-tri-*O*-methyl- and 3 : 4-di-*O*-methyl-D-fructose was described, and the liberated formaldehyde determined as its dimedone derivative. These workers found that a quantitative yield of formaldehyde was frequently difficult to obtain. Experiments on the molar uptake of periodate carried out concurrently gave much higher results than would be expected. This phenomenon was also observed by Hirst and Jones (*J.*, 1949, 1659) and Greville and Northcote (*J.*, 1952, 1945) during the oxidation of certain methylaldoses, and also by Neumüller and Vasseur (*Arkiv. för Kemi*, 1953, 235), while studying the action of periodate on disaccharides at different pH's.

In the present work the methyl ethers of fructose were oxidised at room temperature in the dark, and in view of the earlier anomalous results the formaldehyde obtained was determined both gravimetrically, by Bell's method (*loc. cit.*), and colorimetrically with chromotropic acid (see Eegriwe, *Z. analyt. Chem.*, 1937, **110**, 22); the quantity of periodate consumed was also measured. In order to determine the formaldehyde by the colorimetric method it is necessary first to destroy the excess of periodate, *e.g.* with stannous chloride (Corcoran and Page, *J. Biol. Chem.*, 1940, **146**, 279) or with sodium arsenite (Lambert and Neish, *Canad. J. Res., B.*, 1950, **28**, 83). The procedure finally adopted by the present authors was a modification of a method communicated by Mr. M. W. Rees of Cambridge (unpublished work), to whom they would like to record their thanks. The excess of periodate was removed by sodium hydrogen sulphite solution, and with each set of determinations a standard curve was constructed for glucose, the oxidation of which with liberation of formaldehyde takes place in a few minutes. This curve was linear up to a concentration of approximately 2 μg./ml. of solution. Although difficulties have been reported in the use of chromotropic acid we found good agreement between this method and the gravimetric method in experiments carried out on the same sample. The principal advantages of the colorimetric method are the speed of determination when several sugars are examined and the small amount of sugar, 200—500 μg., required for each estimation.

Although the yields of formaldehyde obtained from the methylated fructoses were reasonably high, yields of 100% were rarely obtained. The exceptions were occasional oxidations in bicarbonate buffer, but results in this medium were variable. The results for 3 : 4 : 6-tri-*O*-methyl- and for 3 : 4-di-*O*-methyl-D-fructose were in agreement with those recorded by Bell *et al.* (*loc. cit.*). The yield of formaldehyde from 1 : 3 : 4-tri-*O*-methylfructose by the colorimetric method was low and did not agree with the theoretical yield recorded by the above authors.

Fructose, 4-*O*-methyl-, 3 : 4-di-*O*-methyl-, and 3 : 4 : 6-tri-*O*-methyl-D-fructose gave nearly theoretical uptakes of periodate, but in every other derivative examined over-oxidation was encountered. With 1 : 4 : 5- and 1 : 4 : 6-tri-*O*-methylfructose the uptake of periodate after 24 hr. was extremely slow and did not exceed 1·4 mol. of periodate with either sugar. There does not appear to be any analogy with the results obtained by Northcote and Greville (*loc. cit.*) from similar methylated glucoses. The latter authors found for 2 : 4 : 6-tri-*O*-methylglucose a periodate consumption of 4·13 mol. of periodate during 294 hr. We consider that, under the mildly alkaline conditions of the experiment, partial enolisation may occur in these two methylated fructoses between $C_{(2)}$ and $C_{(3)}$, and that this is followed by attack by periodate.

TABLE 1. *Determination of formaldehyde gravimetrically.*

Sugar	Buffer	Duration of oxidn., hr.	H·CHO liberated, mol.	H·CHO expected, mol.
Fructose	Phosphate	48	1·70	2·0
	Bicarbonate	48	1·68	—
3 : 4 : 6-Tri-*O*-methylfructose	Phosphate	48	0·88	1·0
	,,	72	0·89	—
	No buffer	72	0·88	—
1 : 4 : 6-Tri-*O*-methylfructose	,,	72	0·10 *	0·0
	Phosphate	72	0·27	—
4-*O*-Methylfructose	No buffer	72	1·40	2·0
	Phosphate	72	1·38	—

* Impure precipitate—low m. p.

TABLE 2. *Determination of formaldehyde colorimetrically.*

Sugar	Buffer	H·CHO liberated, mol. Green filter		Yellow filter		H·CHO expected, mol.
Fructose	Phosphate	1·6	1·7	—	1·72	2·0
	Bicarbonate	1·9	1·4	—	—	—
4-*O*-Methylfructose	Phosphate	1·66	1·76	—	1·70	2·0
	Bicarbonate	—	1·4	—	—	—
3 : 4-Di-*O*-methylfructose	Phosphate	1·58	1·62	—	1·76	2·0
	Bicarbonate	1·76	1·94	—	—	—
4 : 5-Di-*O*-methylfructose	Phosphate	0·83	0·85	0·83	0·90	1·0
	Bicarbonate	0·73	0·80	—	—	—
1 : 3 : 4-Tri-*O*-methylfructose	Phosphate	0·85	0·81	0·78	0·81	1·0
	Bicarbonate	0·79	0·82	—	—	—
3 : 4 : 6-Tri-*O*-methylfructose	Phosphate	0·92	0·89	0·84	0·92,0·90	1·0
	Bicarbonate	0·81	1·00	—	—	—

TABLE 3. *Molar consumption of periodate.*

Sugar	Duration of oxidn., hr.	Uptake, mol.	Expected uptake, mol.
Fructose	48	5·0	5·0
4-*O*-Methylfructose	48	2·7	3·0
	72	2·8	—
3 : 4-Di-*O*-methylfructose	48	2·0	2·0
4 : 5-Di-*O*-methylfructose	48	2·3	2·0
	72	2·5	—
1 : 3 : 4-Tri-*O*-methylfructose	48	1·6	1·0
	72	1·5	—
3 : 4 : 6-Tri-*O*-methylfructose	48	0·8	1·0
1 : 4 : 6-Tri-*O*-methylfructose	24	1·2	1·0
	48	0·9	—
	72	1·3	—
1 : 4 : 5-Tri-*O*-methylfructose	24	1·2	1·0
	48	1·3	—
	72	1·4	—
	168	1·4	—

EXPERIMENTAL

The buffer solutions (pH 7·5, verified in a pH meter) used in the determinations were molar sodium hydrogen carbonate (Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476), and 0·1M-citric acid (1·5 ml.) mixed with 0·2M-disodium hydrogen phosphate (18·5 ml.).

Estimation of Formaldehyde.—(a) *Gravimetric.* Bell's method (*loc. cit.*) was followed, a large excess of periodate being used, together with a crystallisation time of 18 hr.

(b) *Colorimetric.* A solution of the sugar (5 ml.) (sufficient to produce 50—100 μg. of formaldehyde) was mixed with phosphate buffer solution (0·5 ml.; pH 7·5) or with sodium hydrogen carbonate solution (M; 0·1 ml.), and sodium metaperiodate solution (0·3M; 0·1 ml.) in a tared boiling tube, and the stoppered mixture kept in the dark for 48 hr. Sodium hydrogen sulphite solution (s.g. 1·34; 0·2 ml.) was added to destroy excess of periodate, and, after shaking, chromotropic acid (4 : 5-dihydroxynaphthalene-2 : 7-disulphonic acid) (0·1M; 0·5 ml.) added. Concentrated sulphuric acid (20 ml.) was added slowly with cooling in a freezing-mixture. The colour was developed by heating the solution for 10 min. at 85°. After cooling, the volume of the solution was adjusted to 65 ml. Blank experiments were carried out in each determination.

The purple solution was examined in an absorptiometer, green (Ilford 604) and yellow (Ilford 606) filters being used. A calibration curve was constructed for each set of estimations, with glucose as a standard, and straight lines were obtained, with each filter, for quantities of formaldehyde from 10 to 120 μg.

Periodate Uptake.—The amount of periodate consumed was determined by Fleury and Lange's method (*J. Pharm. Chim.*, 1933, **17**, 107, 196). The oxidation was carried out in a bicarbonate buffer (1 g./10 ml. of solution).

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, January 7th*, 1954.]

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*The Reactions of Methyl Radicals with Acetone, Diethyl Ketone, and Di-*tert.*-butyl Peroxide.*

By G. O. PRITCHARD, H. O. PRITCHARD, and A. F. TROTMAN-DICKENSON.

[Reprint Order No. 4765.]

The thermal decomposition of di-*tert.*-butyl peroxide between 130° and 155° has been reinvestigated and the rate constant for the initial fission of the O–O bond found to be $4 \times 10^{16}e^{-39,000/RT}$ sec.$^{-1}$.

The rate constants for the hydrogen abstraction reactions of thermal methyl radicals with di-*tert.*-butyl peroxide, acetone, and diethyl ketone are given by $25 \times 10^{11}e^{-11,700/RT}$, $6{\cdot}4 \times 10^{11}e^{-9500/RT}$, and $6{\cdot}4 \times 10^{11}e^{-8000/RT}$ mole^{-1} c.c. sec.$^{-1}$, respectively.

RALEY, RUST, and VAUGHAN (*J. Amer. Chem. Soc.*, 1948, **70**, 88) have shown that the thermal decomposition of di-*tert.*-butyl peroxide is an essentially non-chain unimolecular process, leading predominantly to the formation of acetone and ethane by the following mechanism :

$$CMe_3{\cdot}O{\cdot}O{\cdot}CMe_3 \xrightarrow{k_1} 2CMe_3{\cdot}O{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CMe_3{\cdot}O{\cdot} \xrightarrow{k_2} COMe_2 + CH_3{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CH_3{\cdot} + CH_3{\cdot} \xrightarrow{k_3} C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

A small amount of methane was formed, probably by the reactions

$$CH_3{\cdot} + CMe_3{\cdot}O{\cdot}O{\cdot}CMe_3 \longrightarrow CH_4 + CMe_3{\cdot}O{\cdot}O{\cdot}CMe_2{\cdot}CH_2{\cdot} \quad . \quad . \quad . \quad (4)$$

$$CMe_3{\cdot}O{\cdot}O{\cdot}CMe_2{\cdot}CH_2{\cdot} + CH_3{\cdot} \longrightarrow CMe_3{\cdot}O{\cdot}O{\cdot}CMe_2{\cdot}CH_2Me \quad . \quad . \quad . \quad . \quad (5)$$

In the gas phase, in the presence of various organic substrates RH, the *tert.*-butoxy-radical is presumed to exhibit no other reactions than (2), which is very fast, but additional reactions of the type (6) can occur.

$$CH_3{\cdot} + RH \xrightarrow{k_6} R{\cdot} + CH_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The purpose of this investigation was to use thermal methyl radicals to study reaction (6) for substances (RH) which are photolytic sources of higher radicals, and whose absorption spectra are such that they themselves would be photolysed if the usual photolytic sources of methyl radicals, dimethylmercury and acetone, were used.

Incidentally, the thermal decomposition of the peroxide was again studied, the rate being measured by the formation of ethane and methane, since the decomposition of each molecule of peroxide leads to the formation of either one molecule of ethane or one of methane.

If RH is acetone, (6) becomes

$$CH_3{\cdot}CO{\cdot}CH_3 + CH_3{\cdot} \longrightarrow CH_3{\cdot}CO{\cdot}CH_2{\cdot} + CH_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The acetonyl radical then reacts with a methyl radical

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot} + CH_3{\cdot} \longrightarrow CH_3{\cdot}CO{\cdot}C_2H_5 \quad \ldots\ldots\ldots (8)$$

to form ethyl methyl ketone. This compound was isolated by Raley, Rust, and Vaughan (*loc. cit.*) from the reaction products of the complete decomposition of the peroxide and was presumably formed by the products of (2) reacting together according to (7) and (8). Consequently, to evaluate correctly the methane formed in (6), the methane formed from the products of (2) must be effectively suppressed. For this reason a high RH concentration is used, and only a small percentage of the peroxide is decomposed. The latter requirement is most important in the investigation of (4), because RH is now di-*tert.*-butyl peroxide itself, and increase of its concentration only serves to increase the rate of (1) and thus the rate of (2) by a proportionate amount.

From the above reaction scheme the rate of methane formation is given by

$$d[CH_4]/dt = R_{CH_4} = k_6[CH_3{\cdot}][RH]$$

and of ethane by

$$d[C_2H_6]/dt = R_{C_2H_6} = k_3[CH_3{\cdot}]^2$$

whence

$$k_6/k_3^{\frac{1}{2}} = R_{CH_4}/R^{\frac{1}{2}}_{C_2H_6}[RH]$$

The plot of log $k_6/k_3^{\frac{1}{2}}$ against $1/T$ gives $E_6 - \frac{1}{2}E_3$ and $A_6/A_3^{\frac{1}{2}}$, where T is the absolute temperature, E is the activation energy, and A is the frequency factor. By using Gomer and Kistiakowsky's values (*J. Chem. Physics*, 1951, **19**, 85) of $E_3 = 0$ kcal./mole and $A_3 = 4{\cdot}5 \times 10^{13}$ mole^{-1} c.c. sec.$^{-1}$ for the recombination of methyl radicals, E_6 and A_6 can be obtained.

Experimental.—The method was to mix measured pressures of the peroxide and ketone in a 2-l. volume surrounded by a steam jacket. This mixture was expanded into a 3-l. reaction vessel immersed in an oil-bath thermostat which could be controlled to $\pm 0{\cdot}1°$ for the period of an experiment. The reaction was terminated by pumping the reactants and products through wide-bore tubing and a liquid-nitrogen trap into a 3-l. bulb. The ethane was collected in liquid-nitrogen traps, and the methane was pumped from the collecting system by a mercury diffusion pump into an analysis system, which consisted of a Töpler pump and a gas burette. When the volume of methane had been measured, the ethane was pumped into the analysis system through traps kept at $-160°$, and its volume measured.

Results and Discussion

In all the runs about 10% of the peroxide was decomposed. When RH was ketone, [RH] was taken as the initial concentration, which was always 1·5—3 times greater than the peroxide concentration. Not more than 0·5% of the acetone reacted, yielding 7—14%

Table 1.

System *	E_1, kcal./mole	A_1, sec.$^{-1}$	k_1, sec.$^{-1}$ (145°)	Source †
Peroxide	38·6	$1{\cdot}9 \times 10^{16}$	$1{\cdot}3 \times 10^{-4}$	This work
Peroxide–acetone	39·5	$5{\cdot}9 \times 10^{16}$	$1{\cdot}3 \times 10^{-4}$	,,
Peroxide–diethyl ketone	39·5	$6{\cdot}8 \times 10^{16}$	$1{\cdot}5 \times 10^{-4}$	,,
Peroxide	39·1	$3{\cdot}2 \times 10^{16}$	$1{\cdot}1 \times 10^{-4}$	*a*
Peroxide	36—40	6×10^{14}—6×10^{16}	1×10^{-4}	*b*
Peroxide–acetone	37	9×10^{14}	$0{\cdot}6 \times 10^{-4}$	*c*
Peroxide–toluene (flow system)	36 ± 1	4×10^{14}—7×10^{14}	$1{\cdot}3 \times 10^{-4}$	*d*
Peroxide–toluene (static system)	34 ± 2	4×10^{13}	$0{\cdot}6 \times 10^{-4}$	*d*
Peroxide	38	7×10^{15}	—	*e*

* Peroxide = di-*tert.*-butyl peroxide.

† *a*, Raley, Rust, and Vaughan, *loc. cit.*; *b*, Brinton and Volman, *J. Chem. Physics*, 1952, **20**, 25; *c*, Jaquiss, Roberts, and Szwarc, *J. Amer. Chem. Soc.*, 1952, **74**, 6005; *d*, Murawski, Roberts, and Szwarc, *J. Chem. Physics*, 1951, **19**, 698; *e*, Lossing and Tickner, *J. Chem. Physics*, 1952, **20**, 907 [this is a composite result of the high-temperature runs (280—350°) of these authors together with the results of *a* and *d*].

of methane of the total methane and ethane formed, and between 2 and 4% of the diethyl ketone reacted, the amount of methane formed varying between 31 and 55%.

When RH was di-*tert.*-butyl peroxide, [RH] was taken as the arithmetic mean of the

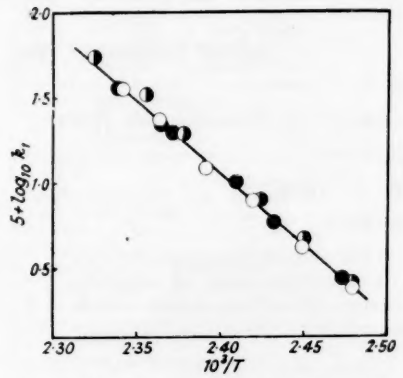
initial and final concentrations of the peroxide, the proportion of methane formed being between 2 and 3%.

The values of E_1, A_1, and k_1 at 145° which have been obtained from Fig. 1 are given in Table 1, together with experimental values of other workers. The present results are seen to lead to a value of E_1 of 39 ± 0·5 kcal./mole, with A_1 about 4×10^{16} sec.$^{-1}$.

In Table 2 the values of E_6, A_6, and k_6 at 182° obtained from Fig. 2 are given, together with the results of other workers.

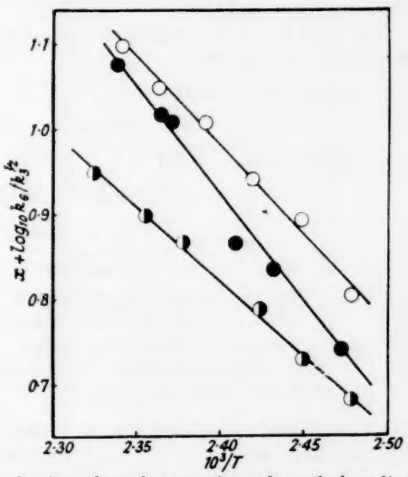
The activation energy obtained for the reaction of methyl radicals with acetone is in excellent agreement with the results of other workers, using both photolytic and thermal methyl radicals. There is a sensible decrease in the activation energy obtained for the reaction with diethyl ketone, in accordance with the general trend exhibited by compounds containing only primary hydrogen atoms, and those containing both primary and secondary hydrogen atoms.

FIG. 1.



Arrhenius plots for the thermal decomposition of di-*tert.*-butyl peroxide: ● alone, ○ in the presence of acetone, and ◑ in the presence of diethyl ketone.

FIG. 2.



Arrhenius plots for reaction of methyl radicals with: ○ Acetone, $x = 1$, ◑ diethyl ketone, $x = 0$, and ● di-*tert.*-butyl peroxide, $x = 1{\cdot}48$.

TABLE 2.

RH *	E_6, kcal./mole †	A_6, mole^{-1} c.c. sec.$^{-1}$	k_6, mole^{-1} c.c. sec.$^{-1}$ (182°)	Source ‡
Acetone	9·5 ± 0·3	$6{\cdot}4 \times 10^{11}$	$1{\cdot}6 \times 10^{7}$	This work
,, ...	9·7 ± 0·1	$4{\cdot}0 \times 10^{11}$	$1{\cdot}0 \times 10^{7}$	*a*
,, ...	9·6 ± 0·4	$3{\cdot}0 \times 10^{11}$	$0{\cdot}8 \times 10^{7}$	*b* §
,, ...	9·5 ± 0·2	$4{\cdot}0 \times 10^{11}$	$1{\cdot}1 \times 10^{7}$	*c*
,, ...	9·5 ± 1·0	$2{\cdot}7 \times 10^{11}$	$0{\cdot}9 \times 10^{7}$	*d*
Diethyl ketone	8·0 ± 0·2	$6{\cdot}4 \times 10^{11}$	$9{\cdot}1 \times 10^{7}$	This work
Peroxide	11·7 ± 0·3	25×10^{11}	$0{\cdot}6 \times 10^{7}$	,,
Peroxide	(15)	(300×10^{11})	$0{\cdot}2 \times 10^{7}$	*e* §

* Peroxide = di-*tert.*-butyl peroxide.

† The probable errors in the activation energies are derived solely from consideration of the deviations of the points from the Arrhenius relationship.

‡ *a*, Trotman-Dickenson and Steacie, *J. Chem. Physics*, 1950, **18**, 1097; *b*, Saunders and H. A. Taylor, *ibid.*, 1941, **9**, 616; *c*, Gomer and Kistiakowsky, *loc. cit.*; *d*, Jaquiss, Roberts, and Szwarc, *loc. cit.*; *e*, Brinton and Volman, *loc. cit.*

§ These quantities were not calculated in this manner by the original authors (see Trotman-Dickenson, *Quart. Reviews*, 1953, **7**, 198).

Kutschke, Wijnen, and Steacie (*J. Amer. Chem. Soc.*, 1952, **74**, 714), using diethyl ketone as a source of ethyl radicals, studied the reaction

$$C_2H_5\cdot + C_2H_5{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_2H_6 + \text{etc.} \quad \ldots\ldots\ldots (9)$$

They found $E_9 = 7{\cdot}4$ kcal./mole, with a steric factor of about 3×10^{-4}. The greater energy of activation required for the methyl (8·0 kcal./mole) than the ethyl (7·4 kcal./mole) radical reaction is surprising, for one would expect that the ethyl radical reaction would require, if anything, a slightly higher activation energy than the methyl radical reaction, because the C–H bond strength in methane exceeds that in ethane by about 5 kcal./mole.

The activation energy for methyl radical attack on di-*tert.*-butyl peroxide is surprisingly high, only methane requiring a higher activation energy of approximately 12·8 kcal./mole (Trotman-Dickenson and Steacie, *J. Phys. Colloid Chem.*, 1951, **55**, 908), whilst other compounds containing only primary C–H bonds have lower activation energies than the 11·7 kcal./mole required for di-*tert.*-butyl peroxide; *e.g.*, ethane 10·4 and 2 : 2 : 3 : 3-tetramethylbutane 9·5 kcal./mole (Trotman-Dickenson, Birchard, and Steacie, *J. Chem. Physics*, 1951, **19**, 163). The reason why this should be is not clear.

One of us (G. O. P.) wishes to thank the Department of Scientific and Industrial Research for a maintenance grant.

UNIVERSITY OF MANCHESTER. [*Received, November 3rd*, 1953.]

Quinones. Part IV. The Elimination of Substituents from 1 : 4-Naphthaquinones.*

By D. B. BRUCE and R. H. THOMSON.

[Reprint Order No. 4867.]

The groups halogen, NHPh, SR, SO_2R, SO_3H, and (in some cases) OH can be removed from positions 2 and 3 of 1 : 4-naphthaquinones by reduction with stannous chloride–hydrochloric acid–acetic acid and subsequent reoxidation with chromic acid. Halogeno-1 : 4-naphthaquinones can be dehalogenated with hydriodic acid.

MANY well-known procedures exist for the preparation of substituted 1 : 4-naphthaquinones but very little has been recorded on the elimination of substituents. Methods for achieving this would be of value in synthetic and degradative work. We previously observed that certain groups can be eliminated from *peri*-hydroxy-1 : 4-naphthaquinones by reduction with stannous chloride (*J.*, 1952, 2759) and we now find that more stringent conditions, *viz.*, refluxing with stannous chloride in hydrochloric acid–acetic acid, provide a general method for the elimination of various substituents (in positions 2 and 3) from 1 : 4-naphthaquinones. The unsubstituted quinone can be readily isolated by direct oxidation of the dilute reaction liquor. In this way halogen, NHPh, SR, SO_2R, and SO_3H groups can be removed, and in some cases OH groups, though with difficulty; but the reaction failed with 3-hydroxy-2-methyl- and 6-bromo-2-hydroxy-1 : 4-naphthaquinone. Some examples are tabulated below.

Three previous instances of this type of reaction have been noted : 1 : 4-naphthaquinol was obtained by Zincke (*Ber.*, 1879, **12**, 1641) by reduction of 2-anilino-1 : 4-naphthaquinone with zinc and alcoholic hydrochloric acid and by Graebe (*Annalen*, 1869, **149**, 6) by treatment of 2 : 3-dichloro-1 : 4-naphthaquinone with tin and hydrochloric acid, and Kehrmann (*Ber.*, 1895, **28**, 345) isolated 1 : 2 : 4-trihydroxynaphthalene from the reduction of 2-hydroxy-3-iodo-1 : 4-naphthaquinone with alcoholic acid stannous chloride.

In the case of the *peri*-hydroxy-1 : 4-naphthaquinones it was postulated that the quinol, formed initially by reduction, tautomerised to a diketone from which the substituent was removed by an acid-catalysed elimination. The same mechanism would account for all the eliminations observed in the present work but it is only necessarily called for in the elimination of anilino-, sulphone, and hydroxyl groups. In the other cases the reaction is probably a direct reduction (or hydrolysis) of an *o*-substituted naphthol (or its keto-isomer) for which parallels exist. *o*-Halogenonaphthols have been reduced by various reagents including stannous chloride (Franzen and Stäuble, *J. pr. Chem.*, 1921,

* Part III, *J.*, 1953, 2910.

103, 382; Fries, *Annalen*, 1930, **484**, 293) and naphtholsulphonic acid can be desulphonated by reduction with sodium amalgam under acid conditions (Friedländer and Lucht, *Ber.*, 1893, **26**, 3031) and by hydrolysis with hydrochloric acid (Nietzki, *Ber.*, 1882, **15**, 305; Leman, *Ann. Chim.*, 1938, **9**, 372). We found that α-naphthol was readily obtained from its 4-sulphonic acid by reduction with stannous chloride. The reduction of hydroxynaphthyl sulphides appears to be new although β-keto-sulphides (which are

Elimination of substituents from 1 : 4-*naphthaquinones.*

(NQ = 1 : 4-Naphthaquinone.)

Derivative	Product	Yield, %
2-Chloro- *	NQ	66
2-Bromo- *	NQ	52
2 : 3-Dichloro- *	NQ	59
2 : 3-Dibromo-	NQ	50
3-Chloro-2-methyl- *	2-Methyl-NQ	91
3-Chloro-2-ethyl- *	2-Ethyl-NQ	90
3-Bromo-2-ethyl-	2-Ethyl-NQ	90
2 : 6-Dibromo-5-hydroxy- *	5-Hydroxy-NQ	47
2 : 3 : 6-Tribromo-5-hydroxy- *	5-Hydroxy-NQ	43
2-Bromo-6-hydroxy-	6-Hydroxy-NQ	93
3 : 6-Dibromo-2-hydroxy-	6-Bromo-2-hydroxy-NQ	65
2-Hydroxy-	NQ	22
3-Chloro-2-hydroxy-	NQ	20
3-Hydroxy-5-methyl-	5-Methyl-NQ	20
2-Anilino-	NQ	40
2-Anilino-3-chloro-	NQ	32
2-Anilino-6-hydroxy-	6-Hydroxy-NQ	50
3-Anilino-6-chloro-	6-Chloro-NQ	58
2-*p*-Tolylthio-	NQ	70
6-Hydroxy-2(or 3)-*p*-tolylthio-	6-Hydroxy-NQ	83
2-Benzenesulphonyl-	NQ	45
2-Toluene-*p*-sulphonyl-	NQ	60
3-Carboxymethylthio-2-methyl-	2-Methyl-NQ	90
2-Sulphonic acid	NQ	47
2-Methyl-NQ-3-sulphonic acid	2-Methyl-NQ	90

* These compounds were also reduced with hydriodic acid, giving the same products.

analogous) have been reduced; *e.g.*, Wahl (*Ber.*, 1922, **55**, 2454) obtained toluene-ω-thiol by treatment of benzyl phenacyl sulphide with zinc and acetic acid. We found that toluene-*p*-thiol was evolved when 1-*p*-tolylthio-2-naphthol was reduced with stannous chloride although the reduction was much slower than that of 2-*p*-tolylthio-1 : 4-naphthaquinone. Sulphones are normally very stable under reducing conditions but several β-keto-sulphones have been reduced. Thus reduction of benzenesulphonylacetone with sodium amalgam gives benzenesulphinic acid and *iso*propyl alcohol, and with zinc and hydrochloric acid benzenethiol is obtained (Otto and Otto, *J. pr. Chem.*, 1887, **36**, 403). However, neither 1-toluene-*p*-sulphonyl-2-naphthol nor 2-toluene-*p*-sulphonylquinol was affected by treatment with stannous chloride. After vigorous reduction of 1 : 2-naphthaquinone, Japp and Klingemann (*J.*, 1893, **63**, 770) isolated some β-naphthol as well as 1 : 2-dihydroxynaphthalene, but Liebermann and Jacobsen (*Annalen*, 1882, **211**, 58) found, and we have confirmed, that stannous chloride reduction of 1 : 2-naphthaquinone yields 3 : 4 : 3′ : 4′-tetrahydroxy-1 : 1′-dinaphthyl. β-Naphthol was not detected. 1-Anilino-2-naphthol was recovered unchanged after similar treatment.

The tautomerisation of 1 : 4-naphthaquinols (lacking *peri*-hydroxyl groups) has never been observed in solution although it appears to occur in certain of the elimination reactions described above. In an attempt to detect such compounds three naphthaquinols were heated in boiling aqueous alcohol in the presence of *p*-nitrophenylhydrazine. However, bis-*p*-nitrophenylhydrazones were not obtained, the products being hydroxyazo-compounds arising from monoketo-structures probably *via* the following route:

The corresponding reactions of α- and β-naphthol with *p*-nitrophenylhydrazine gave small yields of unexpected products; β-naphthol and *p*-nitrophenylhydrazine yielded 2-*p*-nitrophenylazo-1-naphthol, and the corresponding reaction with α-naphthol gave a trace of the same azo-compound but the principal product, dark red needles, m. p. 292—293°, has not been identified. It is known that the reaction of naphthols with phenylhydrazines in the presence of hydrochloric acid gives rise to benzocarbazoles (Japp and Maitland, *J.*, 1903, **83**, 267) but the compound, m. p. 292—292°, is not the nitrobenzcarbazole which would be expected. These reactions are being examined further.

The first reagent employed for the reduction of halogenonaphthols was hydriodic acid (Franzen and Stäuble, *loc. cit.*). Reduction of halogenated 1 : 4-naphthaquinones in the same way eliminates the halogen atoms. This is a satisfactory method for the dehalogenation of 2-alkyl-3-halogeno-1 : 4-naphthaquinones but in other cases the yields are usually poor (*ca.* 20%) and the two-stage stannous chloride reduction and reoxidation is much superior. Some examples are included in the Table.

Experimental

Reduction by Stannous Chloride of Substituted 1 : 4-*Naphthaquinones.*—The following experiment is typical. A mixture of 2 : 3-dibromo-1 : 4-naphthaquinone (0·5 g.), stannous chloride (2 g.), concentrated hydrochloric acid (5 c.c.), and acetic acid (5 c.c.) was refluxed for 30 min., cooled, diluted with water (15 c.c.), and oxidised by addition of chromium trioxide (1 g.) in water (5 c.c.). After cooling in ice, the precipitate was collected. One crystallisation from light petroleum (b. p. 100—120°) gave yellow needles of 1 : 4-naphthaquinone, m. p. 125°. In the case of anilinonaphthaquinones the quinol was extracted from the diluted reaction mixture with ether, and the extract shaken immediately with chromium trioxide in water. Thiols formed by reduction were removed by boiling in an open vessel before oxidation of the quinol.

Miscellaneous Reductions by Stannous Chloride.—(*a*) A mixture of 1-naphthol-4-sulphonic acid (1 g.), stannous chloride (4 g.), concentrated hydrochloric acid (10 c.c.), and acetic acid (10 c.c.) was refluxed for 30 min., diluted with water, and extracted with ether. The extract was evaporated to dryness to yield plates, m. p. and mixed m. p. with α-naphthol, 96° (40%). (*b*) A mixture of 1-*p*-tolylthio-2-naphthol (0·25 g.), stannous chloride (1 g.), concentrated hydrochloric acid (2·5 c.c.), and acetic acid (5 c.c.) was refluxed for 90 min. The odour of toluene-*p*-thiol was soon apparent. The residue [from ether as in (*a*)] was extracted with boiling light petroleum (b. p. 50—60°), to give β-naphthol in leaflets, m. p. and mixed m. p. 122° (35 mg.), and starting material. (*c*) A mixture of 1-toluene-*p*-sulphonyl-2-naphthol (0·28 g.), stannous chloride (1·5 g.), concentrated hydrochloric acid (4 c.c.), and acetic acid (4 c.c.) was refluxed for 2 hr. Starting material (0·27 g.) separated on cooling. Ether-extraction of the diluted filtrate gave a sticky residue smelling faintly of toluene-*p*-thiol, but no β-naphthol was detected.

Reduction by Hydriodic Acid of Halogenated 1 : 4-*Naphthaquinones.*—The following experiment is typical. A mixture of 3-chloro-2-methyl-1 : 4-naphthaquinone (0·3 g.), hydriodic acid (3 c.c.; s.g. 1·7), and acetic acid (3 c.c.) was refluxed for 10 min., cooled, and diluted with water, and the precipitate collected. One crystallisation from light petroleum (b. p. 50—60°) afforded 2-methyl-1 : 4-naphthaquinone in yellow needles, m. p. 106° (66%). In these reductions the crude material was occasionally pink owing to formation of anthocyanidin (cf. Fieser and Fieser, *J. Amer. Chem. Soc.*, 1941, **63**, 1574; Thomson, *J.*, 1953, 1196) which was easily separated owing to its insolubility in light petroleum.

2-*Chloro*-1 : 4-*naphthaquinol.*—2-Chloro-1 : 4-naphthaquinone (0·6 g.) in ether (15 c.c.) was shaken with sodium dithionite (1 g.) in water (10 c.c.) until the colour no longer faded. The ethereal layer was then dried and evaporated *in vacuo*. The residual *quinol* separated from benzene as small crystals, m. p. 153° (decomp.) (Found : C, 61·7; H, 3·5. $C_{10}H_7O_2Cl$ requires C, 61·7; H, 3·6%). The *diacetate* formed needles, m. p. 137—138°, from alcohol (Found : C, 60·2; H, 4·1. $C_{14}H_{11}O_4Cl$ requires C, 60·3; H, 4·0%).

Reaction of Naphthaquinols with p-*Nitrophenylhydrazine.*—(*a*) Hot solutions of 2-chloronaphthaquinol (0·28 g.) in water (50 c.c.) containing concentrated hydrochloric acid (0·5 c.c.), and *p*-nitrophenylhydrazine (0·42 g.) in alcohol (10 c.c.) were mixed, refluxed under nitrogen for 1 hr., and filtered hot. The precipitate (0·13 g., m. p. 260—265°) separated from *o*-dichlorobenzene in dark red crystals, m. p. 274° (Found : C, 58·4; H, 2·9; N, 12·6. $C_{16}H_{10}O_3N_3Cl$

requires C, 58·6; H, 3·1; N, 12·8%). The 2(or 3)-*chloro*-4-p-*nitrophenylazo*-1-*naphthol* gave a blue colour in concentrated sulphuric acid and in aqueous methanolic sodium hydroxide. (*b*) 2-Chloronaphthaquinone (0·19 g.) and *p*-nitrophenylhydrazine (0·15 g.) were dissolved in warm alcohol (10 c.c.). After addition of 3 drops of concentrated hydrochloric acid the product separated rapidly. Crystallisation from *o*-dichlorobenzene yielded material identical with that obtained in (*a*). Hydroxyazo-compounds were similarly obtained from 1 : 4-naphthaquinol and 2-methyl-1 : 4-naphthaquinol. The product from the former (m. p. 280°) did not depress the m. p. of the compound, m. p. 274°, described above.

Reaction of Naphthols with p-*Nitrophenylhydrazine.*—(*a*) A mixture of β-naphthol (1 g.; " AnalaR "), *p*-nitrophenylhydrazine (1 g.), alcohol (25 c.c.), water (50 c.c.), and concentrated hydrochloric acid (1 c.c.) was refluxed for 12 hr. The orange-brown crystalline precipitate obtained (130 mg.; m. p. 225°) crystallised from toluene in light red needles with a green sheen, m. p. 240° (80 mg.) (Found : C, 65·8; H, 3·75. Calc. for $C_{16}H_{11}O_3N_3$: C, 65·5; H, 3·8%). Admixture with 2-*p*-nitrophenylazo-1-naphthol did not depress the m. p. The acetate formed brick-red micro-needles, m. p. 181—182° (Found : C, 64·3; H, 3·9. Calc. for $C_{18}H_{13}O_4N_3$: C, 64·5; H, 3·9%); mixed m. p. with 1-acetoxy-2-*p*-nitrophenylazonaphthalene, 181—182°. Under the same conditions β-naphthol did not react with phenylhydrazine or 2 : 4-dinitrophenylhydrazine. (*b*) The above reaction was carried out upon α-naphthol (1 g.; " AnalaR "). The product (0·18 g.; dark brown; m. p. *ca.* 240°) was chromatographed in *o*-dichlorobenzene on alumina (" Woelm " Acid). On elution with the same solvent a bluish-red band developed from which a *compound*, m. p. 292—293° (dark red needles with a green sheen, from toluene) (35 mg.), was isolated (Found : C, 63·2; H, 3·54; N, 19·1. $C_{12}H_8O_2N_3$ requires C, 63·7; H, 3·55; N, 18·6. $C_{12}H_9O_2N_3$ requires C, 63·4; H, 4·0; N, 18·5%). The compound gave a dark green colour to concentrated sulphuric acid but no colour was produced with alcoholic sodium hydroxide. A second darker zone on the column yielded the azo-dye obtained in (*a*) (17 mg.); the remaining minor bands were not examined.

6-*Nitro*-1 : 2-*benzocarbazole.*—A solution of 1-tetralone *p*-nitrophenylhydrazone (2 g.) in glacial acetic acid (20 c.c.) saturated with dry hydrogen chloride was heated on the steam-bath for 1 hr. Crystals of 3 : 4-*dihydro*-6-*nitro*-1 : 2-*benzocarbazole* (0·67 g.) separated and were collected after cooling. [Dilution of the mother-liquor afforded starting material (0·93 g.).] Recrystallisation from glacial acetic acid gave orange-brown needles, m. p. 277—278° (decomp.) (Found : C, 72·55; H, 4·6; N, 10·3. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·6; N, 10·6%), which gave a blue colour in concentrated sulphuric acid. When the dihydrocarbazole (0·45 g.) and chloranil (0·45 g.) were refluxed in dry xylene (50 c.c.) for 4 hr., 6-*nitro*-1 : 2-*benzocarbazole* separated on cooling. After trituration with dilute aqueous sodium hydroxide it crystallised from *o*-dichlorobenzene in light orange-brown plates, m. p. 318—319° (90%) (Found : C, 73·2; H, 3·7; N, 10·4. $C_{16}H_{10}O_2N_2$ requires C, 73·25; H, 3·8; N, 10·7%), which gave a blue colour in concentrated sulphuric acid.

2-*Benzenesulphonyl*-1 : 4-*naphthaquinone.*—A solution of 1 : 4-naphthaquinone (1 g.) in warm methanol (30 c.c.) was added to sodium benzenesulphinate (1·5 g.) in water (10 c.c.) and methanol (20 c.c.) acidified with 2N-hydrochloric acid (10 c.c.). When the colour had faded and crystals of the quinol began to separate, a solution of ferric chloride (10 g.) in water (50 c.c.) containing hydrochloric acid (1 c.c.) was added. The precipitated *quinone* was collected after some hours and crystallised from aqueous acetic acid. It formed yellow plates, m. p. 192° (75%) (Found : C, 64·65; H, 3·2; S, 10·7. $C_{16}H_{10}O_4S$ requires C, 64·4; H, 3·4; S, 10·7%).

1-*Toluene*-p-*sulphonyl*-2-*naphthol.*—1-*p*-Tolylthio-2-naphthol (0·5 g.) in acetic anhydride (1 c.c.) containing a trace of concentrated sulphuric acid was boiled for 2—3 min., and the solution diluted with glacial acetic acid (20 c.c.). The solution was stirred at 50°, and potassium permanganate (0·5 g.) in water (20 c.c.) added slowly. After addition of a little sodium hydrogen sulphite to destroy the colour, the mixture was poured into ice-water. The precipitated sulphone acetate was boiled for 1 hr. in a mixture of alcohol (10 c.c.) and hydrochloric acid (10 c.c.; 2N) from which 1-*toluene*-p-*sulphonyl*-2-*naphthol* separated on cooling. It formed needles, m. p. 133° (from aqueous alcohol) (60%) (Found : C, 68·4; H, 4·5; S, 11·3. $C_{17}H_{14}O_3S$ requires C, 68·4; H, 4·7; S, 10·75%).

THE UNIVERSITY, OLD ABERDEEN. [*Received, December 7th,* 1953.]

The Chemistry of Fungi. Part XXII. Nidulin and Nornidulin ("Ustin"): Chlorine-containing Metabolic Products of* Aspergillus nidulans.

By F. M. Dean, John C. Roberts, and Alexander Robertson.

[Reprint Order No. 4913.]

The isolation of nidulin and nornidulin ("ustin") from a strain of *Aspergillus nidulans* is described and the empirical formula previously allocated to nornidulin has been confirmed. Nidulin has been shown to be a methyl ether of nornidulin, and the compounds are considered to be chlorinated depsidones. Partial structural formulæ for nidulin and nornidulin are proposed.

From the metabolic liquor of a mould, which had been previously isolated and examined by Kurung (*Science*, **1945**, **102**, 11) who considered it to be a strain of *Aspergillus ustus* (Bain.) Thom and Church, Hogeboom and Craig (*J. Biol. Chem.*, 1946, **162**, 363) isolated, by a counter-current technique, two crystalline products named compound I, m. p. 185—187°, and compound II, m. p. 214—216°, which contained covalent chlorine and were formulated as $C_{21}H_{17}O_6Cl_3$ and $C_{21}H_{18}O_6Cl_2$ respectively. By a simpler method Doering, Dubos, and Noyce (*J. Amer. Chem. Soc.*, 1946, **68**, 725) obtained compound I from the mycelium and metabolic liquors of the same mould and, concluding that this was the major constituent, gave it the name "ustin" and the empirical formula $C_{19}H_{15}O_5Cl_3$; the compound was characterised by the formation of a mono-, m. p. 174°, and a di-methyl ether, m. p. 147°.

It has been reported already that this mould is, in fact, a non-ascosporic strain of *A. nidulans*, and that, when grown under the same or somewhat different conditions from those used by previous workers, the main metabolic product is a compound, m. p. 180°, for which the name nidulin was proposed (Dean, Robertson, Roberts, and Raper, *Nature*, 1953, **172**, 344). Further, nidulin was found to be an *O*-methyl ether of "ustin" and it was suggested that "ustin" should be re-named nornidulin.† In the present paper partial structures for nidulin and nornidulin are developed.

Cultivation of *A. nidulans* at a relatively low temperature for 4—5 weeks yielded a mycelium, which occasionally contained appreciable quantities of nidulin, and a metabolic liquor, from which a small amount of nornidulin was isolated by the method of Doering *et al.* (*loc. cit.*). Thus obtained, nidulin is a colourless, optically inactive compound, m. p. 180°, $C_{20}H_{17}O_5Cl_3$ containing a methoxyl and a hydroxyl group; it readily yields a mono-acetate and a monomethyl derivative. The compound, which has a negative ferric reaction, does not contain a reducing or a carbonyl group. With nidulin the Kuhn–Roth determination of *C*-methyl groups was invalidated by formation of hydrogen chloride on distillation with the acetic acid.

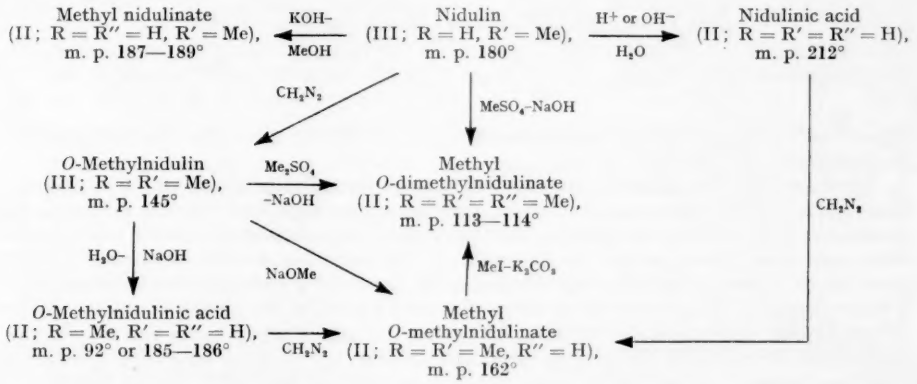
Crystalline nidulin was insoluble in aqueous sodium hydroxide, apparently owing to a surface effect since the amorphous or finely divided compound (formed by pouring an ethanolic solution of the compound into water) was readily soluble in aqueous sodium hydroxide or in aqueous sodium hydrogen carbonate. In cold aqueous alcohol, nidulin behaved on titration as a monobasic acid, a property attributed to the presence of an acidic hydroxyl group rather than to a carboxyl group because, under the same conditions, *O*-acetylnidulin was neutral. The behaviour of nidulin as a dibasic acid on more vigorous treatment with alkali, and the hydrolysis of nidulin to nidulinic acid ($C_{20}H_{19}O_6Cl_3$) without loss of carbon, disclosed a lactone system, the presence of which was confirmed by (*a*) the formation of a hydroxy-ester, methyl nidulinate ($C_{21}H_{21}O_6Cl_3$), on treatment of nidulin with methanolic

* Part XXI, *J.*, 1953, 2434.

† The name "ustin" has priority; but in view of Dr. Raper's revised classification (personal communication and Dean *et al.*, *loc. cit.*) of the mould producing this compound [not produced by authentic *Aspergillus ustus* (Bain.) Thom and Church, unpublished work in this laboratory] and to avoid further confusion we regard the proposed changes as essential.

potassium hydroxide, and (*b*) the production of nidulinic acid and decarbonidulin ($C_{19}H_{19}O_4Cl_3$), a dihydric phenol, when the compound is boiled with excess of sodium hydroxide in aqueous dioxan. Nidulin also behaved as a lactone in reacting with hydroxylamine to form a compound $C_{20}H_{20}O_6NCl_3$, which did not give the expected ferric reaction typical of hydroxamic acids. However, it may well be that the bulk of the rest of the molecule prevents the formation of the hexacovalent iron complex necessary for the production of the colour.

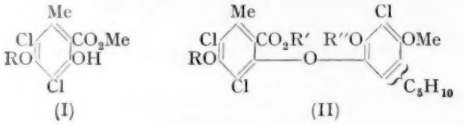
The relations between nidulin, nidulinic acid, and various methylated derivatives are summarised in the annexed scheme.



The chlorine atoms of nidulin are stable to hydrolysis with aqueous or alcoholic sodium hydroxide, to hydrogenolysis over palladium or platinum catalysts, and to the action of Raney nickel alloy and hot alkali according to the method of Schwenk, Papa, and Ginsberg (*J. Org. Chem.*, 1944, **9**, 1). Of the five oxygen atoms in the nidulin molecule, the presence of a lactone, a methoxyl, and a hydroxyl group accounts for four. Further, it seems reasonable to assume that the inert fifth oxygen atom is present in an ether system. Accordingly, from its composition and properties in conjunction with the occurrence of known chlorine-containing depsidones in lichens it seemed probable that nidulin was a depsidone. This assumption is strongly supported by the isolation of methyl 4 : 6-dichloro-*o*-orsellinate (I; R = H) and of methyl 4 : 6-dichloroeverninate (I; R = Me) as degradation products respectively of methyl nidulinate (II; R = R″ = H; R′ = Me) and methyl *O*-methylnidulinate (II; R = R′ = Me; R″ = H). Both degradations were carried out by a sequence of chlorination, reduction, and methanolysis, devised by Nolan, McCann, Manahan, and Nolan (*Sci. Proc. Roy. Dublin Soc.*, 1948, **24**, 319; cf. Zincke and Schurmann, *Annalen*, 1918, **417**, 236) for the fission of diploicin (IV). Further, the remarkably easy fission of methyl *O*-methylnidulinate by nitric acid to give a high yield of methyl dichloroeverninate (I; R = Me) also supported this hypothesis and served to establish the nature and orientation of the substituents of ring A of nidulin (III; R = H; R′ = Me).

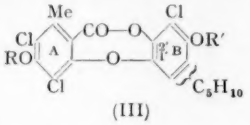
The proposed depsidone structure implies the presence of a second aromatic ring system (ring B) and, although we have not been able to effect a scission of the compound to give the ring-B fragment, the following observations are most simply explained on the view that residue B contains an aromatic system. (*a*) All three chlorine atoms are remarkably stable and, since two have been shown to be in ring A, the third must be attached, presumably, to a second aromatic ring. (*b*) *O*-Methylnidulin (III; R = R′ = Me) reacted smoothly with methanolic sodium methoxide, to give methyl *O*-methylnidulinate (II; R = R′ = Me, R″ = H) which appeared to be phenolic since it was insoluble in sodium hydrogen carbonate solution but dissolved readily in cold aqueous sodium hydroxide. (*c*) In the absence of an aromatic ring (other than ring A), nidulin would be highly unsaturated, whereas it resisted attempts at hydrogenation with Adams catalyst

or Raney nickel and hydrogen at 60 lb./in.^{2} (*d*) In the ultra-violet region nidulin has an inflexion at 323 mμ and a peak at 267 mμ which disappears on decarboxylation and is therefore associated with ring A. If the phenolic hydroxyl of ring B is freed by fission of

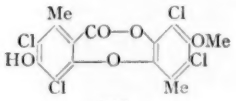


(I)

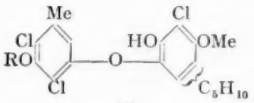
(II)



(III)



(IV)



(V)

the lactone ring, the inflexion is augmented to a peak at 288 mμ consistent with the presence of an aromatic system.

There remain to be allocated one methoxyl group, one chlorine atom, and a C_5 residue. The methoxyl group was placed in the 4'-position by analogy with other depsidones, an orientation confirmed by the positive bleaching-powder reaction of nornidulin (see below). Numerous attempts to isolate the C_5 residue as carbonyl compounds or as simple fatty acids by oxidation of nidulin were unsuccessful, although permanganate oxidation gave a minute quantity of an acid, m. p. 85°, which had a positive fluorescein reaction. None of the possible succinic acids has m. p. 85°, and a number of adipic acids and α-hydroxy-acids which have a similar m. p. were examined but were not identical with the degradation acid (see below). Therefore, in spite of the fact that analogy with known depsidones suggested *n*-pentyl at the 6'-position, we believe that the C_5 residue is present as a ring system attached at the 5'- and 6'-positions of ring B. The third chlorine atom is therefore placed at position 3', with the resulting formula (III; R = H, R' = Me) for nidulin.

In attempts to clarify the nature of the C_5 residue, it was found that nidulin is rapidly attacked by ozone but that *O*-methylnidulin is hardly affected by this reagent; in neither case could any significant product be identified. *O*-Methylnidulin is inert to lead tetra-acetate at 100°, indicating the absence of an active methylene group, whilst on treatment with concentrated nitric acid in acetic acid it affords, not a nitro-compound, but *O*-methyl-dehydronidulin by loss of two hydrogen atoms. Although the dehydro-derivative could not be hydrogenated and does not react with osmium tetroxide and pyridine, it forms an oxide with ozone or perbenzoic acid, suggesting the presence of a tetrasubstituted double bond, and hence the isoprene system ·CHMe·CHMe·CH$_2$· for the C_5 residue. This residue has two methine groups which would facilitate oxidation or nitration (cf. Hass and Riley, *Chem. Reviews*, 1943, **32**, 373) to give intermediates which could yield an olefin, thus accounting for the unusual reaction with nitric acid. The system also has two asymmetric carbon atoms; thus nidulin would be a racemate since it is optically inactive. It is not yet known whether nidulin or any derivative of it can be resolved.

Formula (III; R = H, R' = Me) for nidulin leads to structure (V; R = H) for decarbonidulin which formed a neutral di-*p*-nitrobenzoate and possessed an acidic hydroxyl group responsible for its solubility in aqueous sodium hydrogen carbonate and for its rapid methylation by diazomethane to the phenol *O*-methyldecarbonidulin. A study of the increase in the dissociation constant of phenol caused by chlorine substituents led Tiessens (*Rec. Trav. chim.*, 1929, **48**, 1066) to state that " it is obvious that the presence of two chlorine atoms in *ortho*-positions to the hydroxyl has a predominating effect over all else." Accordingly, *O*-methyldecarbonidulin has been given formula (V; R = Me).

In agreement with Doering *et al.* (*loc. cit.*), we find that nornidulin has the formula $C_{19}H_{15}O_5Cl_3$. Complete methylation of this compound gives a dimethyl ether, m. p. 145° (Doering *et al.* give m. p. 147°), identical with *O*-methylnidulin, and hence the partial structure (III; R = R' = H) for nornidulin (" ustin ") is proposed. Formed by hydration of nornidulin, nornidulinic acid gave a positive bleaching-powder reaction for a resorcinol

derivative, thus confirming the position of the free hydroxyl of ring B of nornidulin with respect to the lactonic system. The monomethyl ether, m. p. 174°, mentioned by Doering *et al.*, is isomeric with nidulin and therefore has structure (III; R = Me, R′ = H).

It appears that nidulin is the first recorded depsidone to be identified as a metabolic product of a fungus grown on a synthetic medium, although compounds of this type are well known as constituents of lichens, and at least three (diploicin, gangaleoidin, and pannarin) contain chlorine (Nolan *et al.*, *loc. cit.*; Davidson, Keane, and Nolan, *Sci. Proc. Roy. Dublin Soc.*, 1943, **23**, 143; Yosioka, *J. Pharm. Soc. Japan*, 1941, **61**, 332). The present discovery is of interest in considerations of phytochemical relations between fungi and lichens.

Succinic acid and mannitol have also been identified as metabolic products of *A. nidulans* (cf. Birkenshaw, Charles, Hetherington, and Raistrick, *Trans. Roy. Soc.*, 1931, *B*, **220**, 153).

The antibiotic properties of nidulin have already been reported elsewhere (Dean *et al.*, *loc. cit.*; cf. Hogeboom and Craig, *loc. cit.*).

Experimental

Isolation of Nidulin.—Stock cultures of *Aspergillus nidulans* (NRRL, No. 2006) (supplied by Dr. Raper) were kept on slopes of Czapek–Dox agar. Fifty flasks each containing 400 ml. of an aqueous solution of Czapek–Dox salts with glucose (4%) and "Marmite" (0·1%), at an initial pH 5·2, were inoculated with a suspension of mould spores in water obtained from a culture at least 15 days old. During 32 days in diffuse daylight at about 13° a rather thin mycelial felt developed, the top of which was green with numerous white or pale-brown spots, whilst the reverse was greyish-green. The substrate was brownish-green with a pH of about 8. Because yields were very variable the method of isolation had to be varied somewhat with different batches. The following account describes the isolation of nidulin from a mycelium which gave a comparatively good yield.

The washed, dried, and powdered mycelial felts (126 g.) from 49 flasks were extracted in Soxhlet apparatus with (*a*) light petroleum (b. p. 40—60°) for 25 hr., (*b*) ether (41 hr.), and (*c*) acetone (34 hr.). In 6 days at room temperature, the light petroleum extract deposited crude, semi-crystalline nidulin (7·3 g.). The brown residue (6·6 g.) left on evaporation of the ethereal extract partly crystallised during 14 days. The combined crystalline products from the two extracts were triturated with cold light petroleum (b. p. 40—60°) and then crystallised from 95% alcohol, giving impure nidulin (6·3 g.), m. p. 174—178°. Repetition of this process followed by crystallisation from light petroleum (b. p. 60—70°; 225 ml. for 1 g. solid) gave nidulin, m. p. 180°, unchanged on recrystallisation from 90% alcohol.

The light petroleum extract, from which crude nidulin had separated, contained fat (2·9 g.) and an intractable, acidic, brown gum (3·8 g.) which yielded positive Liebermann–Burchard and Salkowski reactions and a purple ferric reaction. In addition to nidulin, the ether contained fat (0·2 g.) and an amorphous acidic substance (2·3 g.) devoid of chlorine. On being cooled, the acetone extract yielded mannitol (1·5 g.) which, after being washed with light petroleum (b. p. 40—60°) and ether, crystallised from 90% alcohol (charcoal) in prisms, m. p. 164—168°, forming an acetate, m. p. and mixed m. p. 123—124°.

Isolation of Nornidulin.—The mould was grown on Czapek–Dox medium (25 l.) containing malt extract (0·2%) for 15 days at 28—30°. The filtered culture medium was exhaustively extracted with ether, and the extract was dried and evaporated, leaving a yellow gum (3 g.) which was dissolved in ether (200 ml.), washed with aqueous sodium hydrogen carbonate (3 × 50 ml.), and extracted with 2N-sodium carbonate (3 × 50 ml.). Liberated from this extract by 2N-sulphuric acid (200 ml.), the gummy product was washed with water and ground with a little 2N-sodium carbonate, giving a solid which was dissolved in 50% alcohol (20 ml.). Treatment of this with 2N-sulphuric acid (2 ml.) furnished crystalline nornidulin which separated from aqueous alcohol and then benzene–light petroleum (b. p. 60—80°) in hexagonal plates or prisms (0·6 g.), m. p. 185—186°, $\lambda_{max.}$ 266 mμ (ε 8120), inflection at 323 mμ (ε 746) (Found: C, 53·4; 53·2; H, 3·7, 3·7; Cl, 23·7; MeO, 0. Calc. for $C_{19}H_{15}O_5Cl_3$: C, 53·1; H, 3·5; Cl, 24·8%).

After being extracted with ether the culture liquor was strongly acidified with sulphuric acid and again extracted with ether. When concentrated, this extract deposited crystals which were isolated by decantation and recrystallised from ethyl acetate, giving succinic acid in prisms (0·85 g.), m. p. and mixed m. p. 190—191°, having a positive fluorescein reaction (Found: equiv., 59·3 by titration against 0·1N-sodium hydroxide. Calc. for $C_4H_6O_4$: equiv., 59·0).

Nidulin.—Nidulin crystallises from light petroleum (b. p. 60—70°) in colourless, slender, shining rods, and from alcohol (90%) in rhombs, m. p. 180°, $\lambda_{max.}$ 267 mμ (ε 9010), inflection at 323 mμ (ε 1200), having a negative ferric reaction [Found : C, 54·3, 54·0; H, 4·0, 4·0; Cl, 23·7, 23·4; OMe, 6·9%; *M* (micro-Rast), 463. $C_{19}H_{14}O_4Cl_3$·OMe requires C, 54·1; H, 3·9; Cl, 24·0; OMe, 7·0%; *M*, 443·7]. It is insoluble in water, easily soluble in chloroform, sparingly soluble in 95% alcohol, or benzene, and very sparingly soluble in hot light petroleum (b. p. 60—70°). A 4% solution of the compound in chloroform is optically inactive. Nidulin does not reduce Fehling's solution and does not react with aqueous-methanolic 2 : 4-dinitrophenylhydrazine sulphate.

Addition of water to a solution of nidulin in one equivalent of aqueous sodium hydroxide and cold 95% alcohol did not give a precipitate. Subsequent treatment of this with dilute mineral acid yielded unchanged nidulin, m. p. and mixed m. p. 180° after purification from alcohol.

A solution of nidulin (0·100 g.) in 95% alcohol was neutralised with 0·1N-sodium hydroxide (2·32 ml.) (phenolphthalein as an external indicator) (Calc. for 0·100 g. of a compound $C_{20}H_{17}O_6Cl_3$: 2·25 ml.). To this a further quantity of alkali (2·70 ml.) was added and the solution kept at room temperature overnight, heated under reflux on the steam-bath for 1 hr., cooled, diluted with alcohol (4 ml.), and titrated with standard acid to pH 8·3, with " fractional pH " paper as external indicator because the solution had become pink. The titration indicated the uptake of a further 2·28 ml. of 0·1N-alkali (Calc. for one ester or lactone group : 2·25 ml.). The reaction mixture did not contain chloride ions.

O-*Acetylnidulin* (III; R = Ac, R′ = Me).—A solution of nidulin (0·5 g.) in acetic anhydride (5 ml.) and pyridine (2·5 c.c.) was kept at room temperature for 12 days and poured on crushed ice (100 g.). Two hours later the precipitate (0·53 g.) was collected, washed with water, dried, and crystallised from 95% alcohol, giving O-*acetylnidulin* in plates or slender rods (0·46 g.), m. p. 167—168° (Found : C, 54·4; H, 3·8; Cl, 21·8. $C_{22}H_{19}O_6Cl_3$ requires C, 54·4; H, 3·9; Cl, 21·9%). This derivative was also prepared by acetylation with boiling acetic anhydride containing sodium acetate for 1·5 hr.

Powdered acetylnidulin (produced by pouring an alcoholic solution into water) is insoluble in aqueous sodium hydrogen carbonate but dissolves slowly in a boiling solution of sodium hydroxide.

O-*Methylnidulin* (III; R = R′ = Me).—(*a*) This *ether* was prepared almost quantitatively by treatment of nidulin with an excess of ethereal diazomethane; it separated from 95% methanol in shining, long rods, m. p. 145°, inflection at 298 mμ (ε 1725) [Found, C, 55·4; H, 4·0; Cl, 23·1; OMe, 13·1. Calc. for $C_{19}H_{13}O_3Cl_3(OMe)_2$: C, 55·1; H, 4·2; Cl, 23·3; OMe, 13·6%].

(*b*) A mixture of nidulin (0·44 g.), methyl iodide (1 c.c.), acetone (50 c.c.), and anhydrous potassium carbonate (2·0 g.) was heated under reflux for 6 hr. with the addition of more methyl iodide (0·5 c.c.) after 3 hr. The *O*-methylnidulin (0·2 g.) had m. p. and mixed m. p. 144—145°.

(*c*) By method (*b*), nornidulin (0·4 g.) furnished *O*-methylnidulin (0·35 g.), m. p. and mixed m. p. 144—145° (Found : C, 55·1; H, 4·2; Cl, 23·9; OMe, 13·8%) (cf. Doering *et al.*, *loc. cit.*, who give m. p. 147°).

O-Methylnidulin was not appreciably soluble in boiling sodium hydroxide solution during 3 min.

Reaction of Nidulin with Hydroxylamine.—The pH of a solution of nidulin (1·0 g.), hydroxylamine hydrochloride (2·0 g.), and anhydrous sodium acetate (2·3 g.) in 95% alcohol (50 ml.) and water (25 ml.) was adjusted to 4·8—5·1 with 2N-sodium hydroxide (*ca.* 1·2 ml.). After being heated under reflux on the steam-bath for 4 hr., this mixture was cooled and poured into water (250 ml.), giving a precipitate which was washed free from chloride, dried, and freed from unchanged nidulin by extraction with ice-cold chloroform (6 ml.). Crystallised from aqueous alcohol, the grey, amorphous residue gave a *substance* in slender, colourless prisms (0·20 g.), m. p. 236° (decomp.), which had a negative ferric reaction in alcohol (Found : C, 50·4; H, 4·3; N, 3·1; Cl, 22·9. $C_{20}H_{20}O_6NCl_3$ requires C, 50·4; H, 4·2; N, 2·9; Cl, 22·3%). On being warmed a solution of this compound in acetone reduced Fehling's solution within 5 min.; a control experiment with nidulin did not show reduction.

Nidulinic Acid (II; R = R′ = R″ = H).—A mixture of nidulin (1·5 g.), alcohol (95%; 120 ml.), and 2N-sulphuric acid (180 ml.) was heated under reflux for 17 hr. After part of the alcohol (70 ml.) had been distilled an oil began to separate and the mixture was then kept at −2° overnight. The solid was collected, washed free from acid with water, dried, and crystallised from benzene, giving *nidulinic acid* in diamond-shaped plates (0·9 g.), m. p. 212° (decomp.),

unchanged after a further purification from aqueous alcohol (Found: C, 52·1; H, 4·1; Cl, 22·8; OMe, 5·2. $C_{19}H_{16}O_5Cl_3$·OMe requires C, 51·9; H, 4·1; Cl, 23·0; OMe, 6·7%). Direct titration of this acid gave erratic results, possibly because of partial lactonisation, but the following method was satisfactory. 0·1N-Aqueous sodium hydroxide (6·12 ml.) was added to nidulinic acid (0·1122 g.) in alcohol (10 ml.) and water (10 ml.) and, after being kept in a stoppered flask overnight, the mixture required 0·1N-sulphuric acid (1·26 ml.) for neutralisation to pH 8·3 with pH paper as external indicator (Found: equiv., 231. $C_{20}H_{19}O_6Cl_3$ as a dibasic acid requires equiv., 230·9).

Nidulinic acid is soluble in sodium hydrogen carbonate solution (with slight effervescence), and in alcohol gives a pale-green ferric reaction which is transiently intensified by the addition of water, fading completely in 30 sec.

Methyl Nidulinate (II; R = R″ = H, R′ = Me).—A solution of nidulin (0·80 g.) in methanol (50 ml.) at 40° was treated with methanolic potassium hydroxide (5%; 15 ml.) and then boiled on the steam-bath for 1 min., cooled, diluted with water, and acidified with dilute hydrochloric acid. The copious white precipitate was well washed with water, dried, and crystallised from aqueous methanol, giving *methyl nidulinate* in stout prisms (0·68 g.), m. p. 187—189° (Found: C, 52·9; H, 4·5; Cl, 22·2. $C_{21}H_{21}O_6Cl_3$ requires C, 53·0; H, 4·5; Cl, 22·4%). Powdered methyl nidulinate is soluble in aqueous sodium hydrogen carbonate but does not give a ferric reaction in alcohol.

Methyl O-Methylnidulinate (II; R = R′ = Me, R″ = H).—Nidulinic acid (0·8 g.) and an excess of ethereal diazomethane reacted vigorously and 3 hr. later the solution was decanted from a small flocculent precipitate. Evaporation of the ether with air left a residue which on crystallisation from 95% methanol gave *methyl O-methylnidulinate* in thick hexagonal plates (0·58 g.), m. p. 161°, having a negative ferric reaction $\lambda_{max.}$ 289 mμ (ε 3900) [Found: C, 53·7; H, 5·1; Cl, 22·4; OMe, 17·7. $C_{19}H_{14}O_3Cl_3(OMe)_3$ requires C, 53·9; H, 4·7; Cl, 21·7; OMe, 19·0%].

The same ester was formed by the interaction of *O*-methylnidulin (0·23 g.) and sodium methoxide (from 0·012 g. of sodium) in boiling methanol for 2 hr. and was isolated by neutralisation of the solution with carbon dioxide and evaporation of the solvent. The ester formed pyramid-tipped prisms, m. p. and mixed m. p. 162°, from aqueous methanol.

Powdered methyl *O*-methylnidulinate is soluble in aqueous sodium hydroxide and insoluble in aqueous sodium hydrogen carbonate.

O-*Methylnidulinic Acid* (II; R = Me, R′ = R″ = H).—A mixture of *O*-methylnidulin (0·1 g.), 2N-aqueous sodium hydroxide (10 ml.), and dioxan (10 ml.) was heated on the steam-bath until the solution did not give a precipitate on dilution with water (*ca.* 3 hr.), and after the addition of water (50 ml.) the resulting O-*methylnidulinic acid* was precipitated with 2N-sulphuric acid (20 ml.) and purified from benzene–light petroleum (b. p. 60—80°), forming plates, m. p. 185—186° [Found: C, 53·2; H, 4·7; Cl, 22·0; OMe, 13·0. $C_{19}H_{15}O_4Cl_3(OMe)_2$ requires C, 53·0; H, 4·5; Cl, 22·4; OMe, 13·0%]. In some experiments this acid separated from aqueous dioxan in shining thick parallelograms, m. p. 92° (no sign of decomposition), which solidified at a higher temperature, and then melted at 185°. Recrystallised from benzene, the form of m. p. 92° reverted to plates, m. p. 185°. Both forms were readily soluble in aqueous sodium hydrogen carbonate and on methylation with ethereal diazomethane (or by attempted recrystallisation from hot methanol) gave methyl *O*-methylnidulinate, m. p. and mixed m. p. 162°.

Methyl OO-*Dimethylnidulinate* (II; R = R′ = R″ = Me).—A mixture of nidulin (0·5 g.) or *O*-methylnidulin (0·5 g.), 2N-aqueous sodium hydroxide (20 ml.), and methyl sulphate (1·8 ml.) was heated under reflux for 2 hr., with the addition of more hydroxide (10 ml.) and sulphate (1·8 ml.) after 1 hr. The product was isolated with ether, distilled (240°/0·005 mm.), and crystallised from hot methanol, giving *methyl* OO-*dimethylnidulinate* in prisms (0·21 g.), m. p. 113—114°, insoluble in sodium hydroxide solution [Found: C, 55·0; H, 5·1; Cl, 21·0; OMe, 23·7. $C_{19}H_{13}O_2Cl_3(OMe)_4$ requires C, 54·8; H, 5·0; Cl, 21·1; OMe, 24·6%].

When methyl *O*-methylnidulinate was (0·05 g.) treated with anhydrous potassium carbonate (0·2 g.) and methyl iodide (0·2 ml.) in boiling acetone for 2 hr. the same ester was obtained, having m. p. and mixed m. p. 113—114°.

Decarbonidulin (V; R = H).—A solution of nidulin (1·0 g.) in dioxan (10 ml.) and 2N-aqueous sodium hydroxide (20 ml.) was boiled for 1 hr., cooled, and acidified with dilute sulphuric acid. An ethereal solution of the sticky product was washed (as rapidly as possible) with aqueous sodium hydrogen carbonate solution, to remove nidulinic acid which was regained by acidification, forming prisms (0·2 g.) of m. p. and mixed m. p. 210—212° from benzene–light petroleum (b. p. 60—80°). Spontaneous evaporation of the ether then left *decarbonidulin* as a semi-solid

which on purification from methanol formed prisms (0·2 g.), m. p. 148—149°, $\lambda_{max.}$ 284 mμ (ε 2850), slowly soluble in aqueous sodium hydrogen carbonate (Found, in specimen dried in a vacuum at 80° for 2 hr. : C, 54·8, 54·5; H, 4·3, 4·4; OMe, 7·6. $C_{18}H_{16}O_3Cl_3$·OMe requires C, 54·6; H, 4·6; OMe, 7·4%). Occasionally this compound separated from aqueous dioxan in plates, m. p. 117—118°. The two forms could be quantitatively interconverted by recrystallisation from the appropriate solvents or by seeding. Prepared by the usual method, the *di-p-nitrobenzoate* of decarbonidulin separated from benzene in cream squat prisms, m. p. 195°, insoluble in aqueous sodium hydroxide (Found : N, 3·8; OMe, 4·0. $C_{32}H_{22}O_9N_2Cl_3$·OMe requires N, 3·9; OMe, 4·3%).

O-*Methyldecarbonidulin* (V; R = Me).—When kept with ethereal diazomethane for 3 hr. decarbonidulin (0·2 g. of either form) gave a viscous oil which was dissolved in methanol. Slow evaporation of the solvent left O-*methyldecarbonidulin* in thick prisms (0·11 g.), m. p. 133—135° [Found : C, 55·9; H, 4·9; OMe, 14·0. $C_{18}H_{15}O_3Cl_3(OMe)_2$ requires C, 55·6; H, 4·9; OMe, 14·4%]. This ether was insoluble in aqueous sodium hydrogen carbonate but was soluble in aqueous sodium hydroxide.

Degradation of Methyl Nidulinate to Methyl 4 : 6-*Dichloro-*o*-orsellinate* (I; R = H).—A solution of methyl nidulinate (0·2 g.) in chloroform (7 ml.) was treated with chlorine (0·63 g.) in cold carbon tetrachloride (7 ml.), and the mixture kept at room temperature, in the dark, for 2 days. The solvents and excess of chlorine were removed at 40—50° by a current of dry air, and the residue in acetic acid (12 ml.) was treated with a solution of crystalline stannous chloride (0·7 g.) in a mixture of concentrated hydrochloric acid (10 ml.) and water (8 ml.) at 40°, added in small portions with constant agitation. A pale yellow gum separated and, next day, water (40 ml.) was added and the resulting emulsion extracted with chloroform. The brown oil left on evaporation of the well-washed and dried extracts was heated under reflux with 10% methanolic potassium hydroxide (15 ml.) in hydrogen on the steam-bath for 1 hr. After dilution with water (50 ml.) the cooled solution was acidified with 2N-sulphuric acid (15 ml.), and the sticky product isolated with ether. The ethereal solution, which had been washed with water, was extracted with N-aqueous sodium carbonate and the extracts acidified with dilute sulphuric acid. Crystallised from aqueous methanol (charcoal) and then from 70% methanol, the buff precipitate (62 mg.) gave methyl 4 : 6-dichloro-*o*-orsellinate as a colourless micro-crystalline powder (13 mg.), m. p. 115°, undepressed on admixture with an authentic specimen (Found : C, 40·4; H, 4·0. Calc. for $C_9H_8O_4Cl_2,H_2O$: C, 40·2; H, 3·7%). This compound had the characteristic violet ferric reaction in alcohol and on rubbing became highly electrified (cf. Nolan and Murphy, *Sci. Proc. Roy. Dublin Soc.*, 1941, **22**, 317, and Nolan, Algar, McCann, Manahan, and Nolan, *ibid.*, 1948, **24**, 326).

Degradation of Methyl O-*Methylnidulinate to Methyl* 4 : 6-*Dichloroeverninate* (I; R = Me).—(*a*) Under the foregoing conditions except that the chlorination was continued for 4 days, methyl *O*-methylnidulinate (0·3 g.) gave a crude product, a solution of which in ether (45 ml.) was washed with water and then with 3% aqueous sodium hydrogen carbonate (20 + 10 ml.), and extracted with 1% aqueous sodium hydroxide (20 + 10 + 10 ml.). From the acidified extracts methyl 4 : 6-dichloroeverninate (80 mg.) was isolated and, on crystallisation from aqueous methanol, formed colourless, feathery needles (20 mg.), m. p. 80°, undepressed on admixture with an authentic specimen and having a violet ferric reaction in alcohol [Found : C, 45·7; H, 3·8; Cl, 26·2; OMe, 22·2. Calc. for $C_8H_4O_2Cl_2(OMe)_2$: C, 45·3; H, 3·8; Cl, 26·8; OMe, 23·4%] (cf. Nolan and Murphy, *loc. cit.*, p. 319, who gave m. p. 79—80°).

(*b*) A solution of methyl *O*-methylnidulinate (0·45 g.) in acetic acid (50 ml.) was treated with nitric acid (0·17 ml., *d* 1·4) at room temperature. 15 Minutes later the mixture was diluted with water and extracted with ether. From the combined ethereal extracts which had been washed with aqueous sodium hydrogen carbonate, methyl dichloroeverninate was isolated with the aid of 2N-sodium hydroxide (2 × 25 ml.) and purified from dilute methanol, forming needles (0·2 g.), m. p. and mixed m. p. 82—83°, and having a violet ferric reaction in alcohol.

Oxidation of Nidulin with Potassium Permanganate.—A solution of nidulin (4 g.) in acetone (1 l.) at room temperature was treated with powdered potassium permanganate (10 g.), followed next day with 2N-aqueous sodium carbonate (100 ml.). The filtered mixture was evaporated and the residual aqueous liquor extracted with ether to remove a brown wax from which unchanged nidulin (0·1 g.) was isolated with boiling light petroleum (b. p. 60—80°). After acidification with 2N-sulphuric acid, the parent solution was repeatedly extracted with ether, giving a brown oil, more of which was obtained from the oxides of manganese by clarification in water with sulphur dioxide and extraction with ether. This oil did not distil smoothly but

on being kept at 130°/20 mm. gave a sublimate in colourless plates which on resublimation had m. p. 85° (yield, 2 mg.). This product reacted vigorously with aqueous sodium hydrogen carbonate solution and, with resorcinol and sulphuric acid, gave a positive fluorescein reaction which was destroyed by excess of alkali. The acid, m. p. 85°, depressed the m. p. of the following: (±)-, (+)-, and (−)-β-methyladipic, α-hydroxy*iso*butyric, α-hydroxy*iso*valeric, and (±)-, (+)-, and (−)-α-hydroxy-αβ-dimethylbutyric acid (see below).

O-*Methyldehydronidulin.*—A mixture of *O*-methylnidulin (0·5 g.), acetic acid (6 ml.), and nitric acid (1 ml.; *d* 1·4) was heated on the steam-bath for 5 min., and the product precipitated with water and then crystallised from acetic acid, giving O-*methyldehydronidulin* in long thin prisms (0·4 g.), m. p. 168°, inflection at 298 mμ (ε 1750) [Found: C, 54·6, 54·8; H, 3·6, 3·9; N, nil; Cl, 24·7, 23·1; OMe, 12·8. $C_{19}H_{11}O_3Cl_3(OMe)_2$ requires C, 55·3; H, 3·8; Cl, 23·3; OMe, 13·6%]. This substance could not be hydrogenated with hydrogen and 5% palladium–charcoal at atmospheric pressure.

O-*Methyldehydronidulin Oxide.*—(*a*) A stream of ozone and oxygen was led into a solution of *O*-methyldehydronidulin (0·5 g.) in ethyl acetate (25 ml.) for 15 min. at room temperature. Triturated with water, the white gum left on removal of the solvent in a vacuum gradually solidified and on purification from alcohol gave O-*methyldehydronidulin oxide* in needles and then in colourless prisms (0·1 g.), m. p. 200° [Found: C, 53·3; H, 3·7; Cl, 22·3; OMe, 15·3. $C_{19}H_{11}O_4Cl_3(OMe)_2$ requires C, 53·5; H, 3·6; Cl, 22·6; OMe, 13·2%]. This compound did not react with carbonyl reagents and was only very slowly soluble in boiling aqueous sodium hydroxide. The aqueous liquor from the crude ozonolysis product did not react with 2 : 4-dinitrophenylhydrazine.

(*b*) A solution of *O*-methyldehydronidulin (0·459 g.) in chloroform was mixed with 0·57N-chloroformic perbenzoic acid (20·0 ml.), the volume was made up to 100 ml. with the same solvent, and the mixture was kept at room temperature for 10 days: titration of a sample then indicated the absorption of one atom of oxygen. The mixture was washed successively with 10% aqueous potassium iodide, sodium thiosulphate solution, 2N-aqueous sodium carbonate, and water, dried, and evaporated, giving a pale yellow gum which slowly crystallised. After being washed with ether the oxide separated from alcohol in needles and then in prisms, m. p. and mixed m. p. 200° (Found: C, 53·1; H, 4·1; Cl, 22·4; OMe, 14·8%).

Resolution of (±)-α-*Hydroxy*-αβ-*dimethylbutyric Acid.*—The acid (3·3 g.) (Perkin, *J.*, 1896, **69**, 1457) was added to (−)-brucine (9 g.) dissolved in dry ethyl acetate (200 ml.). On being kept, this deposited (−)-*brucine* (±)-α-*hydroxy*-αβ-*dimethylbutyrate* in prisms (10·7 g.), m. p. 194—197° [Found: N, 5·3; OMe, 12·3. $C_{28}H_{32}O_5N_2(OMe)_2$ requires N, 5·2; OMe, 11·6%]. Fractional crystallisation of this salt from ethyl acetate gave as the less soluble component (−)-*brucine* (+)-α-*hydroxy*-αβ-*dimethylbutyrate*, m. p. 208° (decomp.), $[\alpha]_D^{20}$ −29·65° (*c*, 5 in $CHCl_3$). Liberated from the salt with dilute sulphuric acid and isolated with ether, the (+)-*acid* was distilled [130° (bath)/20 mm.] and then crystallised from light petroleum (b. p. 60—80°), forming plates, m. p. 69—71°, $[\alpha]_D^{20}$ 4·57° (*c*, 5 in $CHCl_3$) (Found: C, 55·0; H, 9·4%; equiv., 128. $C_6H_{12}O_3$ requires C, 54·5; H, 9·2%; equiv., 132). The more soluble salt could not be obtained optically pure but on decomposition furnished the (−)-*acid* which separated from light petroleum (b. p. 60—80°) in plates, m. p. 67—69°, $[\alpha]_D^{20}$ −3·34° (*c*, 5 in $CHCl_3$) (Found: C, 54·5; H, 9·3%; equiv., 132).

Bleaching-powder Tests (cf. Brown, Thesis, Liverpool, 1947).—A filtered, saturated, aqueous solution (0·5 ml.) of bleaching-powder was added to the test substance (5 mg.) after hydrolysis by a mixture of alcohol (0·5 ml.), water (1 ml.), and 2N-aqueous sodium hydroxide (four drops). The following results were obtained: resorcinol, purple (fading rapidly); nidulin and nidulinic acid, very faint pink (fading rapidly); nornidulin, purple (fading rapidly); methyl dichloroeverninate, no colour; methyl dichloro-orsellinate, intense red.

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THE UNIVERSITY, LIVERPOOL.
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The Chemistry of the "Insoluble Red Woods." Part V. Pterocarpin and an Oxidation Product of Homopterocarpin.*

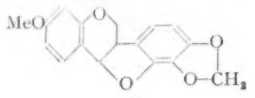
By Alexander Robertson and W. B. Whalley.

[Reprint Order No. 4915.]

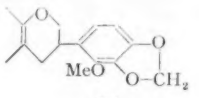
The structure assigned to pterocarpin (*J.*, 1940, 787) has been confirmed by the synthesis of (±)-7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavan (II), *i.e.*, the methyl ether of (±)-dihydropterocarpin.

The oxidation product, $C_{15}H_9O_3(OMe)_3$, of homopterocarpin (*loc. cit.*) has been shown to be 3-hydroxy-7 : 2′ : 4′-trimethoxy*iso*flavan-4-one (VI).

The constitution (I) assigned to pterocarpin from an examination of its degradation products (Part I, *J.*, 1940, 787) has now been supported by a synthesis of (±)-7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavan (II) of which *O*-methyldihydropterocarpin is the (−)-form. 2-Hydroxy-4 : 2′-dimethoxy-3′ : 4′-methylenedioxydeoxybenzoin ((III; R = Me) was prepared from resorcinol and 2-methoxy-3 : 4-methylenedioxybenzyl cyanide by the Hoesch method followed by partial methylation of the product. Reaction of this deoxybenzoin with ethyl formate and sodium gave 2-hydroxy-7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavanone (IV) (cf. Whalley, *J. Amer. Chem. Soc.*, 1953, **75**, 1059) which on dehydration furnished 7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavone. Hydrogenation of this *iso*flavone gave the (±)-flavan (II) which, by comparison of the infra-red absorption spectra, was found to be structurally identical with the natural (−)-*O*-methyldihydropterocarpin; *inter al.*, both compounds showed bands at 1037 cm.$^{-1}$ and 1165 cm.$^{-1}$, characteristic of the methylenedioxy-group, the presence of which is thus definitely established in pterocarpin (cf. Part I, *loc. cit.*).



(I)



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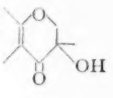

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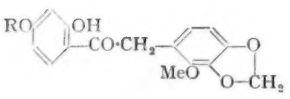

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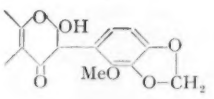

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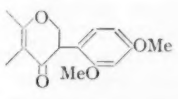

(V)

Formed by the oxidation of *O*-methyldihydrohomopterocarpin, the readily racemised *iso*flavanone (V) gave, on further oxidation, an optically inactive product, $C_{15}H_9O_3(OMe)_3$ (Part I, *loc. cit.*), not identical with 4-hydroxy-7 : 2′ : 4′-trimethoxy-3-phenylcoumarin (Part II, *J.*, 1948, 174), or with 2-hydroxy-7 : 2′ : 4′-trimethoxy*iso*flavanone, the synthesis of which is now described. The compound $C_{15}H_9O_3(OMe)_3$, however, has now been found to be readily dehydrated in a mixture of boiling acetic acid and sulphuric acid, yielding 7 : 2′ : 4′-trimethoxy*iso*flavone, and clearly, therefore, must be 3-hydroxy-7 : 2′ : 4′-trimethoxy*iso*flavanone (VI), the formation of which from (V) is strictly analogous to the oxidation of deoxybenzoins to benzoins under similar conditions (Part IV, *J.*, 1950, 2961).

Experimental

2-Methoxy-3 : 4-methylenedioxybenzyl Cyanide (with G. B. Smith).—Prepared from 2-methoxy-3 : 4-methylenedioxybenzaldehyde (Brownell and Weston, *J. Amer. Chem. Soc.*, 1951, **73**, 4971) (5 g.), hippuric acid (6·5 g.), sodium acetate (3 g.), and acetic anhydride (10 ml.) by the standard method, the *azlactone* (6·7 g.) separated from benzene in bright yellow prisms, m. p. 190° (Found: C, 67·4; H, 4·1; N, 4·3. $C_{18}H_{13}O_5N$ requires C, 66·9; H, 4·0; N, 4·3%).

* Part IV, *J.*, 1950, 2961.

Hydrolysis of this product (6·5 g.) with boiling 10% sodium hydroxide solution (40 ml.) for 5 hr., followed by isolation in the usual manner, furnished 2-methoxy-3 : 4-methylenedioxyphenylpyruvic acid (4·3 g.) which was converted directly into the oxime (4·0 g.). A mixture of the crude air-dried oxime (4·0 g.) and acetic anhydride (10 ml.) was warmed on the steam-bath and, after the initially vigorous reaction had subsided, the solution was diluted with water and 24 hr. later the crystalline precipitate was isolated and purified from alcohol, giving *2-methoxy-3 : 4-methylenedioxybenzyl cyanide* in almost colourless plates (2·1 g.), m. p. 100° (Found : N, 7·1. $C_{10}H_9O_3N$ requires N, 7·3%).

(±)-*7 : 2′-Dimethoxy-3′ : 4′-methylenedioxy*iso*flavan* (II).—The condensation of the aforementioned cyanide (4 g.) with resorcinol (5 g.) in ether (100 ml.) by hydrogen chloride and zinc chloride (2 g.), followed by hydrolysis of the oily ketimine complex with water (50 ml.), gave *2 : 4-dihydroxy-2′-methoxy-3′ : 4′-methylenedioxydeoxybenzoin* (III; R = H) which separated from benzene in needles (2·5 g.), m. p. 165°, having an intense wine-red ferric reaction in alcohol (Found : C, 54·2; H, 4·3. $C_{16}H_{14}O_6$ requires C, 63·6; H, 4·6%). On methylation in acetone by the methyl iodide–potassium carbonate method for 2 hr. this ketone furnished a quantitative yield of *2-hydroxy-4 : 2′-dimethoxy-3′ : 4′-methylenedioxydeoxybenzoin* (III; R = Me) which formed needles, m. p. 127°, from methanol, having an intense red-brown ferric reaction in alcohol (Found : C, 64·4; H, 4·8. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%).

The interaction of this deoxybenzoin (1·8 g.) with ethyl formate (25 ml.) and pulverised sodium (1·5 g.), and the isolation of the product by Whalley's method (*loc. cit.*), gave *2-hydroxy-7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavanone* (IV) (1·2 g.), forming needles, m. p. 188° (decomp.), from ethyl acetate (Found : C, 62·4; H, 4·8. $C_{18}H_{16}O_7$ requires C, 62·8; H, 4·7%). On being boiled in acetic acid during 10 min. this *iso*flavanone was converted quantitatively into *7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavone* which separated from methanol in needles, m. p. 203° unchanged on sublimation at 200°/0·01 mm. (Found : C, 66·2; H, 4·4. $C_{18}H_{14}O_6$ requires C, 66·3; H, 4·3%).

A solution of this *iso*flavone (0·5 g.) in acetic acid (50 ml.) containing Adams's catalyst (0·1 g.) was shaken in hydrogen at atmospheric pressure until one mol. of hydrogen had been absorbed (30 min.). On crystallisation from methanol the gummy product gave (*a*) unchanged *iso*flavone (100 mg.), (*b*) a colourless crystalline solid, m. p. 86°, and (*c*) a non-crystalline residue. Purification of fraction (*b*) from methanol gave (±)-*7 : 2′-dimethoxy-3′ : 4′-methylenedioxy*iso*flavan* (II) in needles (100 mg.), m. p. 86°, insoluble in 2N-aqueous sodium hydroxide and having a negative ferric reaction in alcohol (Found : C, 69·0; H, 6·0. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%). It did not react with 2 : 4-dinitrophenylhydrazine.

The Oxidation Product of (−)-*7 : 2′ : 4-Trimethoxy*iso*flavanone* (V).—A solution of this compound (*loc. cit.*) (0·2 g.), in acetic acid (5 ml.) containing 2N-sulphuric acid (0·5 ml.), was refluxed for 10 min., cooled, and diluted with water, giving a quantitative yield of *7 : 2′ : 4′-trimethoxy*iso*flavone*, m. p. 148° after purification, identical with a synthetical specimen prepared thus. Cyclisation of 2-hydroxy-4 : 2′ : 4′-trimethoxydeoxybenzoin (1·0 g.) with sodium dust (0·3 g.) in ethyl formate (30 ml.) and isolation of product as described previously (*loc. cit.*) furnished *2-hydroxy-7 : 2′ : 4′-trimethoxy*iso*flavanone* (0·3 g.), which separated from ethyl acetate in tablets, m. p. 156° and decomposing with effervescence at *ca.* 180° [Found : C, 65·7; H, 5·3; OMe, 27·6. $C_{15}H_9O_3(OMe)_3$ requires C, 65·5; H, 5·5; OMe, 28·2%]. In boiling acetic acid during 5 min. this *iso*flavanone was converted quantitatively into the *7 : 2′ : 4′-trimethoxy*iso*flavone*, m. p. 148° (cf. Späth and Schläger, *Ber.*, 1940, **73**, 1).

THE UNIVERSITY, LIVERPOOL.

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Nucleotides. Part XXVI. The Methylation of Uridylic Acid* b.

By D. M. Brown, D. I. Magrath, and A. R. Todd.

[Reprint Order No. 4922.]

Repeated methylation of pure uridylic acid *b* with Purdie's reagent gives an apparently uniform material which, when hydrogenated and submitted to acid hydrolysis, yields 2 : 5- and 3 : 5-di-*O*-methylribose and smaller amounts of 2-, 3-, and 5-*O*-methylribose. The method is therefore of no value for the orientation of uridylic acids *a* and *b*. The bearing of these results on the validity of methylation studies as applied to the structural investigation of ribonucleic acids is discussed.

In an earlier paper in this series (Part X, Brown and Todd, *J.*, 1952, 52), possible structures for the ribonucleic acids were discussed and one in which the individual nucleoside residues were linked through the 3′- and 5′-positions by phosphodiester groupings was preferred. Corresponding structures in which 2′ : 5′-phosphodiester linkages, or a mixture of 2′ : 5′- and 3′ : 5′-linkages occurred, could not be excluded on chemical grounds at that time because of the phosphoryl migration which accompanied chemical hydrolysis of ribonucleic acids. The problem was further complicated by the fact that the products of hydrolysis—the four pairs of isomeric *a* and *b* nucleotides—had not been oriented with respect to the position of the phosphoryl group. That the *a* and the *b* nucleotides were the 2′- and the 3′-phosphates of the corresponding nucleosides was clear, but which was 2′- and which 3′- was unknown (Part IX, *idem*, *J.*, 1952, 44). Further work has shown that the ribonucleic acids are to be regarded as *b* : 5′-linked polynucleotides, *i.e.*, that the internucleotidic linkage can be defined in relation to the isolated mononucleotides (Part XIII, Brown, Dekker, and Todd, *J.*, 1952, 2715; Part XXI, Brown and Todd, *J.*, 1953, 2040; Part XXIV, Brown, Heppel, and Hilmoe, *J.*, 1954, 40). It therefore remains only to determine the true location of the phosphoryl group in the *a* and *b* nucleotides to distinguish finally between 2′ : 5′ and 3′ : 5′ as possible positions of the internucleotidic linkage in ribonucleic acids.

The classical method of structural determination in the carbohydrate series—complete methylation followed by hydrolysis and identification of the methylated sugars—is valid only in the absence of group migration, and it was therefore decided in the first instance to study the methylation of a simple nucleotide to find if the method had any value for structural determination in this field. Our interest in this problem was enhanced when Anderson, Barker, Gulland, and Lock (*J.*, 1952, 369) described the methylation of nucleosides and of yeast ribonucleic acid with Purdie's reagent. On hydrolysing the methylated nucleic acid these authors obtained, in rather poor yield, a mixture containing free ribose as well as mono- and di-methylriboses. They concluded that a large amount of chain-branching on sugar occurs in yeast ribonucleic acid, *i.e.*, that the unmethylated ribose originated in branching points where all three hydroxyl groups in a ribofuranose residue are involved in phosphodiester linkages. We had earlier suggested this type of branching on other grounds (Part X, *loc. cit.*), but in view of the known lability of ribonucleic acids or, more generally, of esters of *a* and *b* nucleotides in presence of basic reagents (Part IX, *loc. cit.*), it seemed to us that a study of the methylation of a simple nucleotide would be necessary before the validity of the conclusions of Anderson *et al.* (*loc. cit.*) regarding chain-branching could be assessed.

Crystalline uridylic acid *b*, which was shown by ion-exchange chromatography to be uncontaminated by any of the *a* isomer, was repeatedly methylated with methyl iodide and silver oxide, methanol being used initially as solvent, *i.e.*, the procedure was essentially that used by Anderson *et al.* (*loc. cit.*). The course and extent of methylation at each stage was readily followed by paper-chromatographic examination, since increasing substitution gave products with increasing R_F values in the solvent systems used. In the intermediate stages of the methylation, several chromatographically distinct materials

* Part XXV, *J.*, 1954, 46.

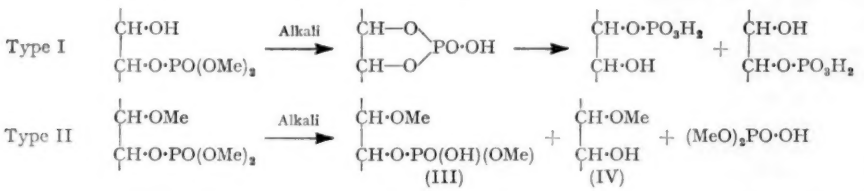
were present, but after fourteen successive methylations the product ran as a single fast-running spot on chromatograms using various solvent systems and methylation appeared to be essentially complete. The methylated product was next hydrogenated to labilise the sugar residue (Levene and Jorpes, *J. Biol. Chem.*, 1929, **81**, 575) and then hydrolysed with 0·5N-sulphuric acid, the conditions necessary for optimum yields of methylated sugars having been determined in preliminary experiments. In addition to **4 : 5**-dihydro-1-methyluracil the crude hydrolysate contained dimethylriboses, a small amount of monomethylriboses, and some acidic phosphorylated methylriboses. A neutral phosphorus-containing substance, fast-running on chromatograms (probably a dimethyl ester of dimethylribose phosphate), was also present in traces; it was evidently an intermediate in the hydrolysis since it occurred in greater amount in short hydrolyses and finally disappeared on prolonged acid treatment, yielding dimethylribose. The hydrolysate was extracted with chloroform and the extract evaporated, giving a mixture of methylated riboses contaminated with **4 : 5**-dihydro-1-methyluracil and a trace of **4 : 5**-dihydrouracil. This mixture was chromatographed on a cellulose column with butanol–water as solvent system; in this way four fractions were obtained, one a dimethylribose fraction and three minor monomethylribose fractions.

The dimethylribose fraction, which was isolated in an analytically pure state, ran as a single spot on paper chromatograms in all the solvents examined. It was clearly distinguishable from **2 : 3**-di-*O*-methylribose but was demonstrably a mixture. On periodate oxidation the material took up *ca.* 1 mol. of oxidant but only 0·65—0·85 mol. of formic acid was liberated even on prolonged oxidation; this is consistent with the view that it was a mixture of **2 : 5**- and **3 : 5**-di-*O*-methyl-ribose, the latter being the major component. Further, on paper electrophoresis in borate buffer, two spots were observed, the more intense migrating towards the anode at a rate comparable with that of ribose, and the other, like the "inert" non-complexing **2 : 3 : 5**-tri-*O*-methylribose, having zero migration. Theoretical considerations relating the structure of sugar derivatives to their electrophoretic behaviour in presence of borate (Foster, *J.*, 1953, 982) would predict precisely this behaviour for **3 : 5**- and **2 : 5**-di-*O*-methylribose respectively. Final confirmation of this view was obtained by the preparation of osazones from the mixture. Treatment with *p*-bromophenylhydrazine furnished two osazones which were separated and purified by chromatography. These were shown to be the *p*-bromophenylosazones of **3 : 5**-di-*O*-methylribose and 5-*O*-methylribose by direct comparison with authentic samples prepared from **2 : 3 : 5**-tri-*O*-methylribose (Barker, *J.*, 1948, 2035) and 5-*O*-methylribose (Levene and Stiller, *J. Biol. Chem.*, 1934, **104**, 299) respectively. Clearly the osazone of 5-*O*-methylribose was derived from **2 : 5**-di-*O*-methylribose in the original material by elimination of the 2-*O*-methyl group. From a consideration of the yields of the two osazones from the mixed dimethylriboses and those obtained in preparing authentic specimens under standard conditions, it appeared that the mixture contained *ca.* 85% of **3 : 5**-di-*O*-methylribose, a value similar to that deduced from periodate oxidation experiments.

Slower-running reducing spots observed on paper chromatograms of the hydrolysis mixture were due to small amounts of 2-, 3-, and 5-*O*-methylribose. These monomethyl sugars were satisfactorily separated on the cellulose column but on the scale of operation used the amounts isolated were too small to permit their complete characterisation. However, their paper chromatographic and electrophoretic behaviour leaves little doubt as to their identity. The first to be eluted from the column was identical in chromatographic and electrophoretic behaviour with authentic 5-*O*-methylribose. The other two were assigned structures on the basis of their chromatographic behaviour and the fact that, since the uridylic acid methylated has a furanose structure, neither could be 4-*O*-methylribose. When submitted to electrophoresis in presence of borate one of them migrated at a rate comparable to that of ribose and **3 : 5**-di-*O*-methylribose. We therefore concluded that it was to be regarded as 3-*O*-methylribose, and have since obtained strong evidence substantiating this formulation (Part XXVII, succeeding paper). The other, like 2-deoxy-L-ribose, travelled much more slowly, and is therefore considered to be 2-*O*-methylribose. Substitution at the 2-position in a sugar leads to a considerable decrease in the rate of migration,

presumably because the preferred formation of a cyclic 1 : 2-*O*-borate complex is prevented and only less stable complexes involving other hydroxyl groups can be formed (Foster, *loc. cit.*; see also Foster and Stacey, *J. Appl. Chem.*, 1953, **3**, 19). It is of interest that the substance we identify as 2-*O*-methylribose appeared to be present (presumably as a result of incomplete methylation) in a sample of 2 : 3-di-*O*-methylribose prepared by methylation of *N* : 5′-ditrityladenosine and subsequent hydrolysis. The monomethylriboses encountered among the hydrolysis products of methylated uridylic acid *b* apparently owe their presence to incomplete methylation, since treatment of the isolated dimethylriboses with acid under the same conditions of hydrolysis did not effect any observable demethylation.

The results of our experiments show clearly that, whatever be the position of the phosphate group in uridylic acid *b*, phosphoryl migration occurs during methylation and hence that the methylation technique is of no value, at least in this form, for orienting the uridylic acids *a* and *b*; it seems reasonable to conclude that it would be equally invalid in the case of the other pairs of *a* and *b* nucleotides. That this should be so was not unexpected, since it was *a priori* likely that the initial action of the methylating agent would be to esterify the phosphoric acid grouping in the uridylic acid giving products which would undergo migration with great ease under the basic conditions of the reaction. We were able to demonstrate that this is so by subjecting uridylic acid *b* to one methylation and examining the products. In addition to unchanged starting material, a second material was present which had the chromatographic and ion-exchange characteristics of a monomethyl ester of uridylic acid. In accordance with this formulation it yielded uridylic acid on treatment with alkali; moreover, when acted upon by ribonuclease, a large proportion was hydrolysed but some remained unaffected. Since ribonuclease attacks specifically the esters of pyrimidine *b* nucleotides and not the *a* isomers (Part XXI, *loc. cit.*) it seems clear that a significant amount of migration had already occurred in one methylation. To unravel the detailed course of the repeated methylation of uridylic acid *b* would be a large undertaking and would, for the purposes of our present work, be unnecessary.



Some evidence regarding the progress of methylation was, however, obtained by studying the action of alkali on the products of methylation at various stages. If the hydroxyl group vicinal to the phosphate residue is unmethylated, *i.e.*, if the methylated material contains a grouping of Type I (above), then treatment with alkali will yield a mixture of two isomeric acids as indicated. If the vicinal hydroxyl is methylated as in Type II, then alkaline hydrolysis will cause fission either to (III) or to (IV) and dimethyl hydrogen phosphate. It was found that, as shown by paper-chromatographic studies, even after 8 successive methylations the products were mainly of Type I; on further methylation, products of Type II became predominant. It is obvious that the possibility of extensive phosphoryl migration exists throughout that part of the methylation process in which the vicinal hydroxyl group remains unmethylated.

The bearing of these findings upon the structural investigation of polynucleotides by the methylation technique (Anderson, Barker, Gulland, and Lock, *loc. cit.*) must now be considered. The structural analogy between the polynucleotides and the esters of simple mononucleotides indicates that phosphoryl migration should occur in methylation of the former as in methylation of the latter. Moreover, migration of the phosphoryl group at $C_{(2')}$ or $C_{(3')}$ would inevitably cause fission of some of the internucleotidic linkages since migration and fission are consequential on each other. Again, the difficulty we experienced in effecting complete methylation of uridylic acid is likely to be even greater in the complex

polynucleotides, so that the occurrence of appreciable amounts of ribose in the hydrolysate of the methylated nucleic acid might well be accounted for on this basis alone. Since each rupture of an internucleotidic linkage would in effect increase the number of " end-groups " capable of yielding dimethylribose, it seems clear that the observed ratios of ribose : monomethylribose : dimethylribose could be explained by a combination of these effects and need not indicate, as Anderson *et al.* concluded, a high degree of chain-branching.

In the absence of much more precise evidence of the homogeneity and molecular weight of a ribonucleic acid and of its methylation product, the results recorded in this paper suggest that the methylation technique as applied by Anderson *et al.* (*loc. cit.*) can lead to no valid conclusions regarding the degree of chain-branching in the original acid.

Experimental

Paper Chromatography and Ionophoresis.—For the paper chromatography of the substances studied the following solvent systems (top layer) were used in ascending chromatograms : A, *n*-butanol–water; B, *n*-butanol–ethanol–water–aqueous ammonia (*d* 0·880) (40 : 10 : 49 : 1, v/v); C, *n*-butanol–acetic acid–water (40 : 10 : 50, v/v); D, pyridine–ethyl acetate–water (1 : 2 : 2, v/v); E, *iso*propanol–water (70 : 30, v/v); F, *iso*propanol–aqueous ammonia (*d* 0·880)–water (70 : 5 : 25, v/v). These solvent systems are designated below by the appropriate capital letter. Nucleotides were located on paper chromatograms by photographing the dried papers in ultra-violet light; phosphates were detected by Hanes and Isherwood's reagent (*Nature*, 1949, **164**, 1107), and sugars by Partridge's aniline hydrogen phthalate reagent (*ibid.*, p. 443). Representative R_F values are given in the Table.

Paper-chromatographic and ionophoretic characteristics of ribose derivatives.

	R_F in solvent system				M_R in 0·1M-sodium borate
	A	B	C	D	
Ribose	0·18	0·27	0·30	0·37	1·00
2-Deoxy-L-ribose	—	—	—	—	0·46
2-*O*-Methylribose	0·34	0·44	0·46	0·49	0·49
3- ,,	0·38	0·45	0·49	0·55	0·90
5- ,,	0·40	0·49	0·51	0·58	0·99
2 : 3-Di-*O*-methylribose	0·53	—	0·64	0·67	0
2 : 5- ,,	0·57	0·65	0·69	0·71	0·02
3 : 5- ,,					0·90
2 : 3 : 5-Tri-*O*-methylribose	0·68	—	—	0·84	0

Paper ionophoresis of sugar derivatives was carried out in an apparatus similar to that described by Flynn and de Mayo (*Lancet*, 1951, 235) in aqueous sodium tetraborate (0·1M) at 210 v. M_R values [equivalent to M_G values as defined by Foster and Stacey (*loc. cit.*) but with ribose and 2 : 3 : 5-tri-*O*-methylribose as reference substances] are given in the Table.

Uridylic Acid b.—The uridylic acid was prepared by acid hydrolysis of yeast ribonucleic acid, followed by ion-exchange chromatography on Dowex-2 resin (formate) (Cohn and Carter, *J. Amer. Chem. Soc.*, 1950, **72**, 2606). The gum obtained on removal of solvent gradually crystallised. After this had been stirred with methanol, *uridylic acid* b was collected and had m. p. 195° (decomp.) (Found, in material dried at 105°/0·2 mm.: C, 33·8; H, 4·5; N, 9·0. $C_9H_{13}O_9N_2P$ requires C, 33·3; H, 4·0; N, 8·7%). As far as we are aware, uridylic acid *b* has not hitherto been isolated in a crystalline state. Levene (*J. Biol. Chem.*, 1920, **41**, 1) gave m. p. 202° (corr.; decomp.) for crystalline " yeast uridylic acid."

An ion-exchange elution diagram (Part XIII, *loc. cit.*) showed only one peak, corresponding in position and optical density ratio (280/260 mμ = 0·32) to uridylic acid *b*. No trace of the *a* isomer was observed. Treatment with dilute acid converted the material into a mixture of the *a* and *b* isomers.

5-O-*Methylribose* p-*Bromophenylosazone*.—5-*O*-Methylribose (0·1 g.), *p*-bromophenylhydrazine (0·35 g., 3·1 mols.), 2N-acetic acid (3 c.c.), and Methylcellosolve (2-methoxyethanol) (1·5 c.c.) were heated together in a stoppered tube on the steam-bath for 3·5—4 hr. On cooling, the reddish oil which had separated solidified and was collected. After trituration with 2N-acetic acid and water, the solid (235 mg.) was dried and dissolved in benzene (25 c.c.). The solution was run on to a column (1·7 cm. diam.) of neutral alumina (25 g.) and washed with benzene and then with benzene containing 2% of methanol to remove dark impurities. Benzene–methanol (19 : 1) moved the product from the top of the column and after extrusion the zone containing

the osazone was extracted with hot methanol (6 × 50 c.c.). Evaporation gave yellow needles (146 mg., 54%). Recrystallisation from benzene and then methanol yielded the pure osazone in long yellow needles, m. p. 178° (Found : C, 43·5; H, 4·3; N, 11·2. Calc. for $C_{18}H_{20}O_3N_4Br_2$: C, 43·2; H, 4·0; N, 11·2%). Levene and Stiller (*loc. cit.*) give m. p. 177°.

3 : 5-*Di*-O-*methylribose* p-*Bromophenylosazone*.—This was obtained from 2 : 3 : 5-tri-*O*-methylribose (0·1 g.) under the conditions described above. The crude product (242 mg. was dissolved in boiling ether (3·5 c.c.) and filtered from acetyl-*p*-bromophenylhydrazine (21 mg.). The ethereal solution was evaporated and the residue dissolved in benzene (10 c.c.) and applied to a column of alumina (25 g.) which was washed with benzene (200 c.c.) and then benzene containing 0·5% of methanol. Benzene containing 1% of methanol (200 c.c.) then rapidly eluted the *osazone* (134 mg., 50%), which crystallised from aqueous methanol in yellow needles, m. p. 176—177°, depressed to 157—164° when mixed with 5-*O*-methylribose *p*-bromophenylosazone (Found : C, 44·8; H, 4·4; N, 11·0. $C_{19}H_{22}O_3N_4Br_2$ requires C, 44·4; H, 4·3; N, 10·9%).

5-O-*Methylribose Phenylosazone*.—The *p*-bromophenylosazones described above proved most convenient for the separation of mixtures of the parent methylated ribose derivatives. Phenylosazones could also be used but were less satisfactory.

5-O-*Methylribose phenylosazone* prepared in the usual way crystallised from methanol in yellow needles, m. p. 152° (Found : C, 62·7; H, 6·3; N, 16·5. $C_{18}H_{22}O_3N_4$ requires C, 63·1; H, 6·5; N, 16·4%).

Methylation of Uridylic Acid b.—The acid (4·0 g.) was methylated at 25—27° as described by Anderson *et al.* (*loc. cit.*) for yeast ribonucleic acid, fourteen additions of silver oxide and methyl iodide being made, with occasional filtration from silver salts and evaporation to dryness. Methanol was added in the initial stages. The product (4·9 g.) was an almost colourless thick syrup [Found, in material dried at 50°/0·2 mm. for 48 hr. : C, 41·6, 43·5; H, 6·0, 5·4; N, 6·3, 7·2; OMe, 28·4, 28·9; NMe, 4·7, 4·3. Calc. for $C_{14}H_{23}O_9N_2P$ (*i.e.*, pentamethyl derivative) : C, 42·6; H, 5·9; N, 7·1; OMe, 31·5; NMe, 7·4%]. The material ran on chromatograms as one spot in all solvent systems except C, in which a trace of slightly slower-running material was observed.

Course of Methylation. At several stages during the methylation small aliquot portions were withdrawn and studied on paper chromatograms. The initial methylation product was clearly uridine methyl hydrogen phosphate (R_F 0·42 in E) (see below.) After three methylations the major components were two neutral fast-running materials (R_F 0·75, 0·84 in E), presumably nucleotide dimethyl esters. When run on chromatograms in solvent system F the whole product from three methylations was converted into material with R_F values 0·35, 0·43, 0·59 (uridine methyl hydrogen phosphate had R_F 0·35 in F). Treatment with 0·5N-sodium hydroxide at 37° overnight largely converted the neutral substance into a material with R_F similar to that of uridylic acid (0·07). This behaviour was still predominant in the product of 8 successive methylations. Thereafter the major component was not affected by the ammoniacal solvent F. The final methylation product (R_F 0·86, 0·84 in C and F respectively), when treated with sodium hydroxide, gave spots (R_F 0·79, 0·43, 0·33 in C; 0·79, 0·65 in F) together with a phosphorus-containing spot showing no ultra-violet absorption (R_F 0·25 in C, 0·51 in F) (dimethyl hydrogen phosphate ?). Phosphorus could not be detected on chromatograms of the highly methylated product by the spray reagent, except after hydrolysis by acid or alkali.

A small sample of uridylic acid *b* was methylated once (as above) and an aqueous solution of the product extracted with chloroform to remove neutral esters. Paper chromatography of the neutralised solution showed that about 40% of a substance having the R_F expected for a monomethyl ester was present. The substance was eluted from a Dowex-2 resin column (280/260 mμ = 0·30) before uridylic acid and uridine-2′ : 3′ phosphate (Part XIII, *loc. cit.*). It was completely converted into uridylic acid by alkali and partly by exhaustive treatment with ribonuclease.

Hydrogenation of Methylated Uridylic Acid b.—Hydrogenation was sluggish but was effected by platinum oxide and hydrogen (Anderson *et al.*, *loc. cit.*) in (*a*) slightly acid aqueous ethanol at atmospheric pressure and 30—50° or (*b*) in the same solvent under 4—5 atm. at room temperature. Hydrogenation was taken to be complete when there was no further decrease in absorption at 260 mμ. The product was a colourless viscous syrup.

Hydrolysis of Hydrogenated Methylation Product.—After many trial hydrolyses, the following conditions were established as affording a maximum yield of dimethylribose. In shorter hydrolyses a substance (R_F 0·80 in C) was observed which gave a positive sugar reaction but a negative phosphate reaction on paper. Phosphorus could, however, be detected in an eluate of

the spot. This material gave rise to dimethylribose and acidic methylated ribose phosphates on further hydrolysis, and was considered to be a dimethyl ester of dimethylribose phosphate.

A solution of the methylated material (2·0 g.) in 0·5N-sulphuric acid (40 c.c.) was heated on the steam-bath for 15 hr. After neutralisation of the product with barium hydroxide solution, barium sulphate was removed, the solution evaporated under reduced pressure, and the residue (2·14 g.) dried at 30—40°/0·1 mm. Extraction with boiling chloroform (3 × 35 c.c.) left an insoluble residue of barium salts of organic phosphates (0·51 g.) which were not further studied. The chloroform extract was evaporated, yielding a reddish-brown syrup (1·64 g.). This material was dissolved in *n*-butanol saturated with water (total, 15 c.c.) and applied to a column (66 × 6 cm.) of cellulose (630 g. of 90-mesh) and eluted with the same solvent (*ca.* 3 l.). Fractions (19 c.c.) were collected at the rate of 80 c.c./hr. and tested for reducing material by spotting them on filter paper and development with the sugar reagent. The exact composition of " key " fractions was ascertained by paper chromatography. Tubes containing the same material were bulked, giving 5 fractions which were evaporated to dryness under reduced pressure. They were examined in order of elution. Initial chromatographic examination showed that no ketoses were present (Partridge and Westall, *Biochem. J.*, 1948, **42**, 238).

Fraction 1. Crystallisation of the semi-solid material (0·5 g.) from ethanol or butanol yielded 4 : 5-dihydro-1-methyluracil in stout colourless needles, m. p. 129°. Anderson *et al.* (*loc. cit.*) give m. p. 129°. In addition to this material, the substance considered to be di-*O*-methylribose dimethyl phosphate was present in traces.

Fraction 2 (*dimethylribose fraction*). The pale yellow gum (185 mg.) was dissolved in a little chloroform, filtered, and evaporated, then taken up in water, filtered, evaporated, and dried to constant weight. The product was a viscous syrup (170 mg.) (Found : C, 47·5; H, 7·6. Calc. for $C_7H_{14}O_5$: C, 47·2; H, 7·9%). A further 25 mg. were obtained by evaporation of adjoining fractions.

The material ran as a compact spot on paper chromatograms with R_F different from that of 2 : 3-di-*O*-methylribose. Ionophoresis in borate buffer gave two spots corresponding to 2 : 5- (weak) and 3 : 5-di-*O*-methylribose (strong) (see Theoretical section).

Quantitative periodate oxidation and formic acid estimation gave the following figures : 26 hr., 0·78 mol./mol. of oxidant consumed; 65 hr., 0·97 (0·66 mol. of formic acid); 288 hr., 1·28 (0·85) indicating that the 3 : 5-isomer predominated. It is of interest that no formic acid could be detected on chromatograms of the dimethylribose fraction by the periodate spray technique of Buchanan, Dekker, and Long (*J.*, 1950, 3162).

No appreciable demethylation occurred when the material was heated at 100° for 15 hr. in 0·5N-sulphuric acid.

A portion of the syrup (160 mg.) was treated with *p*-bromophenylhydrazine as described above for the preparation of *p*-bromophenylosazones from 5-*O*-methyl- and 2 : 3 : 5-tri-*O*-methyl-ribose. The crude product, a yellow powder (320 mg.), was chromatographed in benzene on neutral alumina. Development with benzene containing increasing amounts of methanol (cf. above) yielded two pure products. The first eluted (216·5 mg.) was recrystallised from aqueous methanol and had m. p. 174—175° (155 mg.) undepressed in admixture with authentic 3 : 5-di-*O*-methylribose *p*-bromophenylosazone. The second, obtained in much smaller amount (30 mg.), had m. p. 177—178° after recrystallisation and was identified as 5-*O*-methylribose *p*-bromophenylosazone by m. p. and mixed m. p.

Fraction 3. The yellowish syrup (7 mg.) was examined by paper chromatography. In all solvents examined it had R_F identical with that of 5-*O*-methylribose, and it was identical with this sugar in ionophoretic behaviour (M_R value).

Fraction 4. The semi-solid material (33 mg.) was extracted with chloroform, leaving an insoluble residue which, when sublimed at 200°/0·1 mm., gave colourless crystals of 4 : 5-dihydrouracil m. p. 274°. (Traces of this substance were also present in Fractions 3 and 5.) The chloroform extract gave a yellowish syrup (19 mg.) on evaporation. On the basis of its chromatographic and ionophoretic behaviour it was identified as 3-*O*-methylribose.

Fraction 5. Extraction with boiling chloroform yielded a syrup (20 mg.) which it was concluded was essentially 2-*O*-methylribose. Its ionophoretic mobility was the same as that of 2-deoxy-L-ribose, and of another sugar present in hydrolysates of partially methylated *N* : 5′-dirityladenosine (cf. Theoretical section).

On paper chromatograms, satisfactory separation of mixtures of Fractions 3, 4, and 5 could only be achieved by using solvent system D.

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Nucleotides. Part XXVII. The Structures of Adenylic Acids* a *and* b.

By D. M. Brown, G. D. Fasman, D. I. Magrath, and A. R. Todd.

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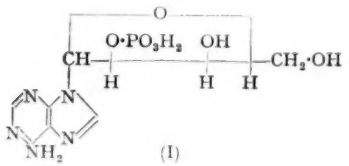
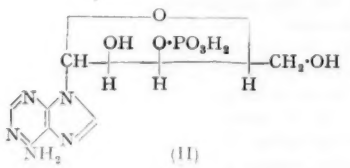
Adenosine-2′ phosphate has been synthesised by a route which avoids phosphoryl migration and is thus unambiguous. The synthetic product is identical with adenylic acid *a* obtained from ribonucleic acids. It follows that adenylic acid *b* is adenosine-3′ phosphate, a conclusion independently reached by *X*-ray crystallographic analysis.

The chemical hydrolysis of ribonucleic acids yields a mixture of eight mononucleotides consisting of 4 pairs of isomeric *a* and *b* nucleotides, each derived from one and the same nucleoside (Carter and Cohn, *Fed. Proc.*, 1949, **8**, 190, and subsequent papers). Distinguished from the nucleoside-5′ phosphates by their stability towards periodate, they were formulated as nucleoside-2′ and -3′ phosphates, although not necessarily respectively (Brown and Todd, Part IX, *J.*, 1952, 44). This conclusion was rendered more certain, in the case of the isomeric adenylic acids (I and II), by their simultaneous synthesis by phosphorylation of 5′-*O*-trityladenosine (Part IX, *loc. cit.*). Precise determination of the structures of the isomeric nucleotides is necessary, *inter alia*, for rigid definition of the position of the internucleotidic linkage-points in the polyribonucleotides.

In the pyrimidine nucleotide series, consideration of physical properties (density of aqueous solutions, p*K* values, and ultra-violet and infra-red absorption spectra) has led several investigators to the conclusion that cytidylic acid *a* and *b* are cytidine-2′ and -3′ phosphate respectively (Loring, Hammell, Levy, and Bortner, *J. Biol. Chem.*, 1952, **196**, 821; Cavalieri, *J. Amer. Chem. Soc.*, 1952, **74**, 5804; Fox, Cavalieri, and Chang, *ibid.*, 1953, **75**, 4315; Michelson and Todd, *J.*, 1954, 34). Cytidylic acid *b* has been related chemically to uridylic acid *b* (Brown, Dekker, and Todd, *J.*, 1952, 2715), so that, if the orientations reached for the cytidylic acids are accepted, the structures of the uridylic acids follow. Clearly, however, rigid chemical confirmation would be desirable, since the evidence quoted above is merely circumstantial.



(I)



(II)

The chemical properties of the isomeric acids severely limit the available means of structural determination by degradation. The *a* and the *b* nucleotides undergo interconversion in acidic but not in alkaline media (Cohn, *J. Amer. Chem. Soc.*, 1950, **72**, 2811; Part IX, *loc. cit.*; Loring, Bortner, Levy, and Hammell, *J. Biol. Chem.*, 1952, **196**, 807), while their monoesters are labile in both acid and alkaline solution, phosphoryl migration and loss of the esterifying group occurring simultaneously (Brown and Todd, Part X, *J.*, 1952, 52). These interconversions proceed through the intermediate cyclic nucleoside-2′ : 3′ phosphate (Brown, Magrath, and Todd, *J.*, 1952, 2708).

Phosphoryl migration clearly invalidates earlier conclusions regarding the structures of yeast adenylic and guanylic acids (Levene and Harris, *J. Biol. Chem.*, 1932, **98**, 9; 1933, **101**, 419), since the degradations used depended on acid hydrolysis to remove the aglycone. Doherty (Abs. 118th Meeting Amer. Chem. Soc., 1950, 56c) obtained the *same* products from both adenylic acid *a* and *b* by acid-catalysed alcoholysis, a result undoubtedly to

* Part XXVI, preceding paper.

be ascribed to phosphoryl migration. Migration of the phosphoryl group was also observed when uridylic acid *b* was methylated with Purdie's reagent (Brown, Magrath, and Todd, preceding paper). This result was considered to depend on the action of the basic reagent on the methyl esters formed initially; the method, in any event, was not applicable to determining the location of the phosphoryl group.

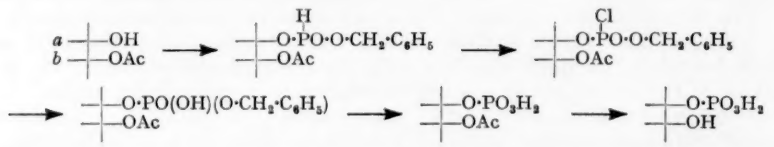
Khym, Doherty, Cohn, and Volkin have recently described in a preliminary communication (*J. Amer. Chem. Soc.*, 1953, **75**, 1262) the application of a modified hydrolytic procedure to the structural determination of adenylic acids *a* and *b*. Short treatment of either acid with the sulphonic acid resin Dowex-50 in the acid form gave a mixture of ribose-2 and ribose-3 phosphates which were separable by ion-exchange chromatography. The proportions of the two sugar phosphates differed in each case, and according to these authors "the amount of each is found to be proportional to the average amount of each resin-absorbed adenylic acid isomer existing during the hydrolysis period (*ca.* 30 seconds, 100°)." No detail of the experiments was given, but the conclusion drawn from them was that adenylic acids *a* and *b* are respectively adenosine-2′ and adenosine-3′ phosphates. Although this conclusion was probably justified, it clearly rested on arguments depending on relative rates of phosphoryl migration and hydrolysis. We have sought a solution of the structural problem using processes by which phosphoryl migration could be experimentally excluded. Only by imposing this condition could complete unambiguity be attained.

By using a synthetic route it was hoped that a general method might be evolved, applicable equally to the case of the other nucleotide isomers. Further, it was expected that the synthetic method would yield nucleosides oriented with respect to substituents in the 2′- and 3′-positions which would be of value in other nucleotide studies in progress in these laboratories. The results of the present chemical work have already been briefly reported, together with concomitant *X*-ray crystallographic studies (Brown, Fasman, Magrath, Todd, Cochran, and Woolfson, *Nature*, 1953, **172**, 1184). Both the chemical and the physical studies showed that adenylic acids *a* and *b* are adenosine-2′ and -3′ phosphate respectively, in agreement with the conclusions of Khym *et al.* In the present communication, the chemical studies are described in detail.

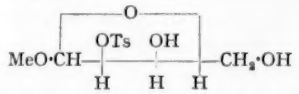
In principle, our aim was to obtain an *x* : 5′-di-*O*-substituted adenosine, which by phosphorylation and removal of protecting groups would yield only one of the two adenylic acids. By further substituting the same disubstituted adenosine with a group which would be incapable of migration during further chemical degradation it was hoped to show unambiguously the position of that group and hence the position of the phosphoryl group in the synthetic adenylic acid. Owing to the *trans*-arrangement of the hydroxyl groups at $C_{(3')}$ and $C_{(5')}$ in the ribofuranose residue of the nucleosides, the formation of 3′ : 5′-bridged (*e.g.*, benzylidene) derivatives has not been possible (Brown, Haynes, and Todd, *J.*, 1950, 3299). Recourse was had to acylation methods. Monoacetylation of 5′-*O*-trityladenosine gave a product which could not be purified, although removal of the trityl group and counter-current separation yielded a crystalline mono(2′ or 3′)-*O*-acetyladenosine. This material was not further studied. Acetylation of 5′-*O*-acetyladenosine (Brown, Haynes, and Todd, *loc. cit.*) in the same way led to a mixture of mono-, di-, and triacetyladenosines from which one, and only one, crystalline diacetyladenosine could be isolated by counter-current distribution.

The di-*O*-acetyladenosine was phosphorylated with *O*-benzyl phosphorous *OO*-diphenylphosphoric anhydride (Corby, Kenner, and Todd, *J.*, 1952, 3669), yielding a diacetyladenosine benzyl phosphite which, by the action of *N*-chlorosuccinimide (Kenner, Todd, and Weymouth, *J.*, 1952, 3675), followed by very mild hydrolysis with aqueous pyridine, gave diacetyladenosine benzyl hydrogen phosphate. Hydrogenation to remove the benzyl group, followed by deacetylation with methanolic ammonia, gave the nucleotide. The intermediates which were, as expected, gums or amorphous materials were not fractionated, so that loss of nucleotidic products was minimised. The final product was obtained in crystalline form and was identified as adenylic acid *a*, by comparison with authentic specimens in melting point, chromatographic and ion-exchange characteristics, *X*-ray powder photographs, and infra-red spectra (cf. Part IX, *loc. cit.*). Moreover, the solution

obtained at the deacetylation stage, but before crystallisation of the free acid, was shown by ion-exchange chromatography to contain *only* adenylic acid *a*, there being no trace of the *b* isomer. Individual steps in the synthetic method, which is set out in partial formulæ below, were designed to avoid phosphoryl migration. The production of one, and only one, adenylic acid indicates its success, since phosphoryl migration at any stage would necessarily have led to a mixture of two isomeric acids.



If the position of the phosphoryl group in the ribofuranose residue of adenylic acid *a* is denoted by *a* and that in the *b* isomer by *b*, then it follows that the diacetyladenosine used was *b* : 5′-di-*O*-acetyladenosine. This, with toluene-*p*-sulphonyl chloride, gave in high yield the crystalline *b* : 5′-di-*O*-acetyl-*a*-*O*-toluene-*p*-sulphonyladenosine, converted by the action of methanolic ammonia into *a*-*O*-toluene-*p*-sulphonyladenosine. It was intended to convert this toluene-*p*-sulphonyladenosine, or its diacetate, into a toluene-*p*-sulphonylribose, or a derivative of the latter, by hydrolysis or alcoholysis. In model experiments 2′ : 3′ : 5′-tri-*O*-acetyladenosine was treated with 1% methanolic hydrogen chloride at 65° and with 5% acid at 100°. In each case methyl ribopyranoside could be isolated in high yield, the ring size being determined by periodate titration. On use of the former conditions, the diacetyltoluene-*p*-sulphonyladenosine gave only toluene-*p*-sulphonyladenosine. The more vigorous conditions gave methyl *a*-toluene-*p*-sulphonylriboside. This substance was stable to periodate. Clearly it was either a 2- or 3-*O*-toluene-*p*-sulphonylribofuranoside (*viz.*, III) or else 3-*O*-toluene-*p*-sulphonylribopyranoside, but no further conclusions could be drawn from periodate titration results as to the location of the toluene-*p*-sulphonyl group.



(III)

(Ts = *p*-$C_6H_4Me\cdot SO_2$·)

Acid hydrolysis was next studied and it became clear that the diacetyltoluene-*p*-sulphonyladenosine was very stable. Conditions which readily yielded ribose from adenosine only deacetylated it. More vigorous acidic conditions did degrade the compound and gave solutions containing adenine and a reducing substance which had the expected chromatographic characteristics of a toluene-*p*-sulphonylribose. The material could not, however, be isolated in a pure state and, indeed, it appeared that considerable decomposition of the sugar had occurred. An attempt to oxidise the crude product with bromine and isolate the toluene-*p*-sulphonylribonic acid as its amide also failed. The methyl toluene-*p*-sulphonylriboside proved equally resistant to acid hydrolysis.

Several examples of increased stability of glycosides and glycosyl halides, toluene-*p*-sulphonylated in the 2- or the 3-position, have been recorded (Reynolds, *J.*, 1931, 2626; Bernoulli and Stauffer, *Helv. Chim. Acta*, 1940, **23**, 615; Percival and Percival, *J.*, 1938, 1585; Percival and Zobrist, *J.*, 1952, 4306). Reynolds (*loc. cit.*) noted the considerably enhanced stability of triacetyl-2-*O*-toluene-*p*-sulphonylglucosyl chloride over the corresponding triacetyl-3-*O*-toluene-*p*-sulphonylglucosyl bromide (Freudenberg and Ivers, *Ber.*, 1922, **55**, 929). We, ourselves, found that methyl 2-*O*-toluene-*p*-sulphonyl-α-glucoside was very stable toward aqueous sulphuric acid and we were unable by this means to convert it into the free sugar. Moreover, Percival and Zobrist (*loc. cit.*) noted that when methyl 3 : 5-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonylxyloside was treated with 1% methanolic hydrogen chloride at 70° removal of the acetone residue occurred almost exclusively without ring expansion, only traces of pyranoside being formed.

The accumulated evidence seemed to point to the conclusion that we were dealing

with 2-toluene-*p*-sulphonyl derivatives, in which case the methyl *a*-toluene-*p*-sulphonylriboside must have retained the furanose form (III). This proved to be the case. Methylation with Purdie's reagent, removal of the toluene-*p*-sulphonyl group by reductive fission with sodium amalgam, and acid hydrolysis (which now proceeded smoothly), yielded a mixture of methylated sugars. Paper chromatography showed that the product was a mixture of mono- and di-methylriboses, in which the latter predominated; no trimethylribose was present. The mixture was fractionated by chromatography on a cellulose column. We have discussed elsewhere the identification of various methylated ribose derivatives by means of paper chromatographic and ionophoretic methods (preceding paper); the same techniques were applied to the present problem. The monomethylriboses were eluted from the column in two fractions. The first contained 5-*O*-methylribose, and the substance formulated (preceding paper) as 3-*O*-methylribose. The second, very small, fraction contained a sugar which could only be distinguished with difficulty from 2-*O*-methylribose on paper chromatograms in the usual solvent systems. The chromatographic method of Bayly and Bourne (*Nature*, 1953, **171**, 385), depending on conversion into *N*-benzylglycosylamines, however, readily distinguished the substance from 2-*O*-methylribose. We formulate it as 4-*O*-methylribose and attribute its formation to a very small amount of pyranoside present in the methyl toluene-*p*-sulphonylriboside (cf. Percival and Zobrist, *loc. cit.*). This accords well with the absence of this substance in the products of methylation and hydrolysis of *a*-toluene-*p*-sulphonyladenosine, the only discernible monomethylribose in that case being 3-*O*-methylribose.

The dimethylribose fraction appeared to be essentially 3 : 5-di-*O*-methylribose. 2 : 3- and 2 : 5-Di-*O*-methylribose were entirely absent and only a trace of another substance was present. This is formulated as 3 : 4-di-*O*-methylribose (cf. Percival and Zobrist, *loc. cit.*) on the basis of its ionophoretic characteristics and its absence in the methylated sugars derived from methylated *a*-*O*-toluene-*p*-sulphonyladenosine.

The dimethylribose fraction was treated with *p*-bromophenylhydrazine and yielded an osazone, in good yield, identical with an authentic specimen of 3 : 5-*O*-dimethylribose *p*-bromophenylosazone (preceding paper).

The isolation of 3 : 5-di-*O*-methylribose uncontaminated with any 2-substituted ribose proves that it was derived from methyl 2-toluene-*p*-sulphonylribofuranoside (III). It follows rigidly that the original toluene-*p*-sulphonylated diacetyladenosine was 3′ : 5′-di-*O*-acetyl-2′-*O*-toluene-*p*-sulphonyladenosine and hence that adenylic acid *a* is adenosine-2′ phosphate (I). It follows, further, that adenylic acid *b* is adenosine-3′ phosphate (II) (cf. Brown and Todd, Part IX); independent proof has also been obtained by *X*-ray crystallographic analysis of adenylic acid *b* (Brown, Fasman, Magrath, Todd, Cochran, and Woolfson, *loc. cit.*).

Convincing evidence has already been presented for the view that the ribonucleic acids are *b* : 5′-linked polynucleotides (Brown, Dekker, and Todd, *loc. cit.*; Brown and Todd, *J.*, 1953, 2040; Brown, Heppel, and Hilmoe, *J.*, 1954, 40). The evidence presented in this paper, coupled with the probable identification of the *b* isomers of the pyrimidine nucleotides with the corresponding nucleoside-3′ phosphates, makes it virtually certain that the ribonucleic acids are polynucleotides in which successive nucleoside residues are linked through the 3′ and the 5′ positions by phosphodiester groupings. Final proof is now being sought by extension of the method of structural determination here described to the pyrimidine nucleotides. From physical measurements of the type earlier applied to the cytidilic acids Cavalieri (*J. Amer. Chem. Soc.*, 1953, **75**, 5268) has recently obtained data on the isomeric adenylic acids from which he concluded that the acids have the structures demonstrated here.

Experimental

R_F values quoted, except where otherwise stated, are from paper chromatograms run in *n*-butanol–acetic acid–water (40 : 10 : 50) on Whatman No. 1 paper.

2′(or 3′)-O-*Acetyladenosine*.—5′-*O*-Trityladenosine (4·14 g.) was dissolved in hot, dry pyridine (105 c.c.), and the solution cooled to 0°. After addition of acetic anhydride (0·9 c.c., 1 mol.) with stirring, the solution was set aside at room temperature overnight. The solution

was poured into ice-water, and the gummy product collected and refluxed with 80% acetic acid for 20 min. Evaporation below 35° left a residue which was extracted with boiling water (250 c.c.) for ½ hr. The combined filtrates from this and two further similar extractions of the residue gave, on evaporation under reduced pressure, a colourless resin. This material was fractionated by counter-current distribution with ethyl acetate–water (23 transfers; 94-c.c. phase). The nature of the material present in each tube was determined by paper chromatography. In addition to adenosine (R_F 0·29) and 2′ : 3′-*O*-diacetyladenosine (R_F 0·94) a monoacetyladenosine (R_F 0·63) was present (in tubes 5—9). Evaporation of the monoacetyladenosine fraction yielded a gum (0·6 g.) which was dissolved in a minimum of ethanol. Careful addition of light petroleum (b. p. 80—100°) furnished colourless needles of 2′(or 3′)-O-*acetyladenosine*, m. p. 173—175° (Found, in material dried at 105°/1 mm.: C, 46·6; H, 5·0. $C_{12}H_{15}O_5N_5$ requires C, 46·7; H, 4·9%).

3′ : 5′-*Di*-O-*acetyladenosine*.—5′-*O*-Acetyladenosine (2·67 g.; Brown, Haynes, and Todd, *loc. cit.*), dried for 2 days at 50°/0·1 mm., was dissolved in warm, dry pyridine (254 c.c.) with exclusion of moisture, then cooled to 0°. Acetic anhydride (0·9 c.c., 1·1 mols.) was added with shaking, and the solution was set aside overnight. Removal of solvents below 50° followed by evaporation with added ethanol and toluene left a thick gum. This was dissolved in 80% acetic acid (267 c.c.), and the solution boiled under reflux for 20 min., in order to remove any *N*-acetyl groups. Removal of acetic acid below 50° left a brown gum which was separated into its components by counter-current distribution in an 11-stage, 95-c.c. phase machine, using 22 transfers. The solvents were ethyl acetate and water. 5′-*O*-Acetyl- and 2′ : 3′ : 5′-tri-*O*-acetyl-adenosine were recovered from the appropriate tubes. The contents of tubes 6—16 were combined and the solvent was removed under reduced pressure. The residual clear gum was dissolved in ethanol, and light petroleum (b. p. 80—100°) (or pentane) was added to opalescence. Slow crystallisation occurred when the solution was set aside in the ice-chest for several weeks. 3′ : 5′-*Di*-O-*acetyladenosine* formed colourless ball-like aggregates of needles (0·81 g., 23%), m. p. 146—147° (Found, in material dried at 0·1 mm.: C, 47·9; H, 5·2; N, 19·7. $C_{14}H_{17}O_6N_5$ requires C, 47·8; H, 4·9; N, 19·9%).

For a larger-scale preparation (from 21 g. of 5′-*O*-acetyladenosine) a 100-stage automatic counter-current apparatus was used (20·5-c.c. phase). The gum was dissolved in the bottom phase of the first 11 tubes, and 88 transfers were carried out. The diacetyladenosine was recovered from tubes 35—64. Outside these limits the product was contaminated with 5′-*O*-acetyl- and tri-*O*-acetyl-adenosine.

Adenosine-2′ Phosphate (*Adenylic Acid* a).—3′ : 5′-Di-*O*-acetyladenosine (0·1 g.) was dissolved in a mixture of dry benzene (15 c.c.) and dry methyl cyanide (3 c.c.). *O*-Benzyl-phosphorous *OO*-diphenylphosphoric anhydride (2 mols.; Corby, Kenner, and Todd, *loc. cit.*) in benzene was added, followed by 2 : 6-lutidine (0·31 c.c., 2 mols.), and the mixture was shaken vigorously. The materials dissolved slowly during 1·5 hr. After a further 30 min., solvents were removed under reduced pressure and the residue was dissolved in chloroform (25 c.c.). The solution was washed successively with water (5 c.c.), saturated sodium hydrogen carbonate solution (5 c.c.), and water (5 c.c.), and then evaporated, the last traces of water being removed by azeotropic distillation with benzene under reduced pressure. The colourless resin (0·15 g.) was dissolved in benzene (5 c.c.) and the solution poured into *cyclo*hexane (100 c.c.). The colourless, gummy 3′ : 5′-di-*O*-acetyladenosine-2′ benzyl phosphite which separated was dried *in vacuo* (0·139 g., 97%) and had R_F 0·78.

The above material was dissolved in dry methyl cyanide (10 c.c.), *N*-chlorosuccinimide (0·043 g., 1·1 mols.) was added, and the solution was set aside for 2 hr. Water (0·3 c.c.) and pyridine (1·0 c.c.) were added to the yellow solution, and the mixture was set aside overnight. Removal of solvents under reduced pressure, followed by re-evaporation with ethanol, yielded a gum which was dissolved in water (10 c.c.). The solution was brought to pH 1 with dilute hydrochloric acid and rapidly extracted with chloroform (5 × 10 c.c.), and the chloroform extract washed with water (5 c.c.). Evaporation of the chloroform left a gum from which the last traces of water were removed by azeotropic distillation with benzene. The crude 3′ : 5′-di-*O*-acetyladenosine-2′ benzyl phosphate (0·087 g., 59%) had R_F 0·70, but was contaminated with a small amount of unidentified impurity of R_F 0·36.

The above benzyl phosphate was dissolved in water (10 c.c.) and ethanol (2 c.c.), and the solution hydrogenated overnight in presence of platinum oxide (5 mg.) and palladium–charcoal (15 mg.). After being heated to 100°, the solution was filtered and the catalyst washed with more solvent. Evaporation to dryness yielded 3′ : 5′-di-*O*-acetyladenosine-2′ phosphate as a gum (0·067 g., 55%; R_F 0·33). The material was dissolved in half-saturated methanolic

ammonia (10 c.c.) and set aside overnight. Removal of solvents gave crude ammonium adenosine-2′ phosphate. It was dissolved in water (100 c.c.), and the solution brought to pH 8 and run on to a column (2·5 cm.^{2} × 3 cm.) of Dowex-2 resin (formate form). The column was washed with water (200 c.c.), and the product was eluted with N-formic acid (100 c.c.). The solution was evaporated to small volume under reduced pressure and finally freeze-dried, yielding a colourless foam (0·04 g.). Recrystallisation from a few drops of water gave pure adenosine-2′ phosphate (14 mg.), m. p. 183°, R_P 0·04 (Found, in material dried at 50° over P_2O_5: N, 18·7. Calc. for $C_{10}H_{14}O_7N_5P,1{\cdot}5H_2O$: N, 18·7%). The substance had an infra-red spectrum and an *X*-ray powder diagram identical with those of natural and synthetic adenylic acid *a*. It did not depress the m. p. (183°) of an authentic specimen and was unaffected by sodium metaperiodate (Part IX, *loc. cit.*). It had R_P 0·68 in Carter's sodium phosphate–*iso*amyl alcohol solvent system (*J. Amer. Chem. Soc.*, **1950**, **72**, **1466**) (authentic adenylic acid *a*, 0·69). The crude ammonium salt (3 mg.; above) was chromatographed on a Dowex-2 (formate) ion-exchange column which had been calibrated with respect to the elution positions of adenylic acids *a* and *b*. Only one peak was observed corresponding to adenylic acid *a*, so that in the product before crystallisation only one of the isomeric acids was present.

Adenosine-5′ Phosphate.—In initial experiments to test the feasibility of the above reaction scheme, adenosine-5′ phosphate was synthesised from 2′ : 3′-di-*O*-acetyladenosine (0·1 g.) by the same procedure. Crystallisation from water gave the pure acid (0·030 g., 30%) (Found, in material dried at 50°: N, 19·4. Calc. for $C_{10}H_{14}O_7N_5P,H_2O$: N, 19·2%). The synthetic acid had m. p. 192° and did not depress the m. p. (189°) of an authentic sample of adenosine-5′ phosphate. It gave an *X*-ray powder photograph identical with that of an authentic specimen. The infra-red spectrum of the anhydrous substance (dried at 110°) as a mull in Nujol was different from that recorded earlier for adenosine-5′ phosphate (Part IX) but was identical with that obtained for a recrystallised specimen of adenosine-5′ phosphate prepared *via* 3′ : 5′-*O*-benzylidene adenosine (Brown, Haynes, and Todd, *loc. cit.*) and dried in the same way. The infra-red absorption bands (μ) (w = weak, m = medium strength, *s* = strong) were: 3·03, 3·15 m (doublet), 5·91 s, 6·40 w, 6·66 m, 7·45 m, 7·65 w, 7·83, 7·93 w (doublet), 8·2, 8·46, 8·64 m, 8·90 s, 9·20 m, 9·45, 9·90, 10·55 s, 11·15, 11·45, 11·6, 11·85 w, 12·94, 13·43, 13·9 m. The difference between this spectrum and that recorded earlier is doubtless due to the fact that the earlier determination was carried out on hydrated material.

3′ : 5′-*Di*-O-*acetyl*-2′-O-*toluene*-p-*sulphonyladenosine.*—Dry 3′ : 5′-di-*O*-acetyladenosine (0·454 g.) was dissolved in anhydrous pyridine (11·1 c.c.) at 40°, and the solution cooled to 0°. Toluene-*p*-sulphonyl chloride (0·744 g., 1·1 mols.) was added with shaking, and the yellow solution set aside at room temperature overnight. Water (10 c.c.) and cold saturated sodium hydrogen carbonate solution (50 c.c.) were added and the solution was extracted rapidly with ice-cold chloroform (3 × 50 c.c.). This extract was washed with ice-cold saturated sodium hydrogen sulphate solution and then with water. Removal of solvent, together with remaining traces of water, by distillation with benzene under reduced pressure gave colourless crystals. Recrystallisation from chloroform gave the *product* (0·545 g., 84%) as hair-like needles, m. p. 78—81° (Found, in material dried at 50°/0·1 mm. over P_2O_5: C, 49·9; H, 4·9; N, 13·3; S, 6·2. $C_{21}H_{25}O_8N_5S$ requires C, 49·9; H, 4·6; N, 13·8; S, 6·3%). The compound was evidently dimorphous since crystallisation from a small amount of ethanol gave rosettes of needles, m. p. 144° (Found, C, 49·9; H, 4·6%). The substance had R_P 0·87.

2′-O-*Toluene*-p-*sulphonyladenosine.*—(*a*) The above diacetyl derivative (26 mg.) was dissolved in half-saturated methanolic ammonia (1 c.c.) and set aside at 0° overnight. Evaporation to dryness and crystallisation of the residue from ethanol gave the *product* in irregular transparent plates, m. p. 222—223° (Found, in material dried at 110°/0·1 mm. over P_2O_5: C, 48·8; H, 4·5. $C_{17}H_{19}O_6N_5S$ requires C, 48·5; H, 4·5%).

(*b*) The diacetyl derivative (0·2 g.) was boiled under reflux in 2% methanolic hydrogen chloride (20 c.c.) for 12 hr. The acid was neutralised with diazomethane and then the solution evaporated to dryness. The residual gum was dissolved in ether (10 c.c.) and methanol (1 c.c.) and filtered. Evaporation of the filtrate and crystallisation of the residue (0·133 g.) from ethanol gave 2′-*O*-toluene-*p*-sulphonyladenosine, m. p. 222—223°, undepressed in admixture with the material prepared by methanolic ammonia deacetylation (Found: C, 48·5; H, 4·5%). The substance had R_F, 0·74.

Methanolysis of 3′ : 5′-*Di*-O-*acetyl*-2′-O-*toluene*-p-*sulphonyladenosine.*—The tosyl derivative (0·5 g.) was dissolved in 5% methanolic hydrogen chloride solution (15 c.c.) and heated for 6 hr. at 100° in a sealed Pyrex tube. The solution was neutralised by addition of ethereal diazomethane. After evaporation of ether and dilution to 20 c.c. with dry methanol the

solution was passed through a column (6 × 1 cm. diam.) of Dowex-50 resin (acidic form) which had been washed with dry methanol. After washing with more methanol (25 c.c.), the eluate and washings, now free of adenine, were combined and evaporated. The gum was dissolved in methanol, and the solution filtered and evaporated. The gummy product (0·193 g., 61%) was dried for 8 hr. at 10^{-5} mm. and consisted of *methyl* 2-O-*toluene*-p-*sulphonylribofuranoside* contaminated with a trace of the pyranoside (Found: C, 48·6; H, 5·8. $C_{13}H_{18}O_7S$ requires C, 49·0; H, 5·7%). On periodate oxidation the substance consumed 0·02 mol. of oxidant per mol.

Methanolysis of 2′:3′:5′-*Tri*-O-*acetyladenosine.*—Under the conditions used above, triacetyladenosine (0·2 g.) and 5% methanolic hydrogen chloride (15 c.c.) yielded methylribopyranoside as an oil (0·082 g., 98%) (Found: C, 44·0; H, 7·6. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·4%). It consumed 2·02 mols. of metaperiodate per mol.

The product (Found: C, 43·9; H, 7·1%) obtained by using 1% methanolic hydrogen chloride under reflux for 6 hr. consumed 1·6 mols. of periodate per mol.

Acid Hydrolysis of 3′:5′-*Di*-O-*acetyl*-2′-*toluene*-p-*sulphonyladenosine.*—A large variety of conditions was studied, with 4—10% aqueous hydrochloric acid at 100°. The degree of hydrolysis was followed by paper chromatography, by observing the disappearance of toluene-*p*-sulphonyladenosine and the formation of adenine together with a substance which gave a pink spot (R_F *ca.* 0·8) with the aniline hydrogen phthalate reagent, presumably 2-*O*-toluene-*p*-sulphonylribose. Working up by the methods used above for the methyl ribosides yielded dark oils giving variable analytical values. The product gave no *p*-bromophenylosazone or -hydrazone, nor could oxidation to the ribonolactone and conversion into the ribonamide be effected.

Methyl 2-O-*Toluene*-p-*sulphonyl*-α-*glucoside.*—The 4:6-*O*-benzylidene derivative (Robertson, *J.*, 1935, 1193) was boiled under reflux for 12 hr. with oxalic acid (15 g.) in acetone (450 c.c.) and water (50 c.c.). Barium carbonate was added and the precipitate removed by filtration. The filtrate was evaporated, to remove acetone, and the residual aqueous solution extracted with ether. Evaporation of the aqueous layer left a gum which crystallised from ethyl acetate in rosettes of needles. *Methyl* 2-O-*toluene*-p-*sulphonyl*-α-*glucoside* (1·9 g.) had m. p. 138—139° (Found: C, 48·5; H, 6·1. $C_{14}H_{20}O_8S$ requires C, 48·3; H, 5·8%). The substance was recovered unchanged (m. p. 136°) after being heated with 0·33N-sulphuric acid for 8 hr. at 70°.

Methylation of Methyl 2-O-*Toluene*-p-*sulphonylriboside*—Methyl 2-*O*-toluene-*p*-sulphonylriboside (0·19 g.) was shaken in methyl iodide (0·5 c.c.) with silver oxide (0·15 g.) for 17 hr. at 25°. Removal of silver salts by filtration and evaporation to dryness yielded a gum which was dissolved in methyl iodide (1·5 c.c.) and shaken with three further portions of silver oxide (2 × 0·07 g., and 0·15 g.) added at 12-hr. intervals. Evaporation of the filtered solution gave the methylated material as a colourless resin.

The methylation product was dissolved in methanol (6·6 c.c.) and water (3 c.c.), and 4% sodium amalgam (6 g.) added during 5 hr. with vigorous stirring at 35°. After being stirred for a further 6 hr., the solution was set aside overnight and then decanted through a filter. The residue was washed with more methanol, and filtrate and washings were neutralised with 2N-sulphuric acid. The solution was evaporated and the residue dried at 35°/0·1 mm. Extraction with chloroform (5 × 10 c.c.) and evaporation of the extract yielded the methylated methyl ribofuranoside as a colourless oil (0·115 g.).

This material was heated on the steam-bath in 0·5N-sulphuric acid (3 c.c.) for 5 hr. and the solution was then neutralised with saturated barium hydroxide solution. Barium sulphate was removed by filtration and washed with hot water. Filtrate and washings were reduced to small bulk, filtered, and evaporated to dryness. The pale orange syrup (0·103 g.) was dried at 35°/0·5 mm. Chromatographic examination of this material indicated that the syrup consisted largely of dimethylated ribose together with a smaller quantity of monomethylated ribose. No ribose or trimethylribose was present.

Separation and Identification of the Methylated Ribose Derivatives.—Chromatography using butanol–water as solvent on a column (6 cm. diam.) of cellulose (300 g.; 90-mesh), in accordance with the technique described in the preceding paper, permitted fractionation of the above methylated sugar mixture. Three fractions were obtained and are described below in order of elution.

Fraction 1 (*dimethylribose fraction*). The colourless syrup (0·064 g.) consisted almost entirely of a substance whose behaviour on paper chromatography and ionophoresis was identical with that of 3:5-di-*O*-methylribose. No 2:5-di-*O*-methylribose was present. A trace of a substance was observed with R_F 0·67 in pyridine–ethyl acetate–water and M_R

0·22 in 0·1M-sodium borate (3 : 5-di-*O*-methylribose has R_F 0·71 and M_R 0·90). The material is regarded as 3 : 4-di-*O*-methylribose (see Theoretical section).

A solution of the syrup (0·06 g.) in Methylcellosolve (2-methoxyethanol) (0·83 c.c.) and 2N-acetic acid (1·62 c.c.) was heated with *p*-bromophenylhydrazine (0·197 g.) in a stoppered tube at 100° for 4·5 hr. After cooling to room temperature, the product was collected and then triturated with cold 2N-acetic acid (3 × 2 c.c.) and then water. The dried solid (0·122 g.) was dissolved in benzene and purified by chromatography on a column of neutral alumina (1·7 cm. diam.; 15 g.) as described in the preceding paper. The crystalline product (0·106 g., 61%) separated from aqueous methanol in fine, yellow needles, m. p. 176—177°, undepressed on admixture with authentic 3 : 5-di-*O*-methylribose *p*-bromophenylosazone.

Fraction 2. The colourless syrup (18 mg.) consisted of a mixture of two sugars identified as 3- and 5-*O*-methylribose by their ionophoretic and paper-chromatographic characteristics in a number of solvents.

Fraction 3. This fraction (3·6 mg.) consisted of a colourless syrup with a trace of solid material. Chromatographic examination showed the presence of a single reducing sugar of slightly lower R_F (0·47 in pyridine–ethyl acetate–water) than 2-*O*-methylribose (0·49). On ionophoresis, it had M_R 0·49 in 0·1M-sodium borate, identical with that of 2-*O*-methylribose. The two sugars were clearly distinguished by applying the benzylamine technique (Bayly and Bourne, *loc cit.*). 2-*O*-Methylribose gave a spot, detected with the ninhydrin and aniline hydrogen phthalate spray reagents, with R_F 0·84 (pyridine–ethyl acetate–water), while the new substance, in common with 3- and 5-*O*-methylribose, had R_F 0·95. The sugar is tentatively regarded as 4-*O*-methylribose.

Methylation of 2′-O-*Toluene*-p-*sulphonyladenosine.*—2′-*O*-Toluene-*p*-sulphonyladenosine (from 0·11 g. of diacetyl derivative) was methylated by the technique used for the methylation of uridylic acid *b* (preceding paper). Fifteen treatments with silver oxide and methyl iodide failed to effect complete methylation. The pale resin obtained was reduced with 4% sodium amalgam (2 g.) in aqueous methanol, and the product hydrolysed with 0·5N-sulphuric acid, as above. The solution was neutralised with sodium hydrogen carbonate and evaporated to small bulk, much of the methyladenine separating as a brown oil. The aqueous phase was studied on chromatograms and by ionophoresis. Only two reducing substances appeared to be present. The first was identified as 3 : 5-di-*O*-methylribose by comparison with specimens prepared above and previously. The other reducing sugar, which constituted about 65% of the mixture, was readily distinguished from 5-*O*-methylribose and behaved identically with the substance formulated as 3-*O*-methylribose. Its presence, in association with 3 : 5-di-*O*-methylribose, is strong confirmation of the correctness of the structure ascribed to it in the preceding paper (p. 1443).

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, December 23rd,* 1953.]

Acylation and Allied Reactions catalysed by Strong Acids. Part XII. The Allyl and Some Related Cations.*

By H. Burton and D. A. Munday.

[Reprint Order No. 5045.]

Allyl phenyl ether is not cleaved by acetylium perchlorate but undergoes *C*-acetylation to *p*-allyloxyacetophenone. Reactions with allyl, but-2-enyl (crotyl), and cinnamyl perchlorates generally lead to the formation of complex products: the cations themselves also give "polymeric products." Cinnamoyl perchlorate reacts with anisole under a variety of conditions giving high yields of *p*-methoxyphenyl styryl ketone.

It has been postulated by Alexander ("Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, 1950, p. 42) that the benzyl and allyl cations are formed with particular ease and that the ions are stabilised by resonance. Burton and Praill (*J.*, 1951, 522) showed that the benzyl cation can be formed very easily by the action of acetylium perchlorate on an aryl benzyl ether, but found later (*J.*, 1953, 827) that when the cation was derived from benzyl perchlorate in an inert solvent (nitromethane) of relatively high dielectric constant it was markedly unstable and underwent "polymerisation": it was also noted that oxygen was probably incorporated into the polymer at some stage. In view of the well-known reactivity of allyl halides under all conditions of nucleophilic substitution and their similarity to benzyl halides, we have investigated the behaviour of allyl phenyl ether and some related ethers towards the acetylium ion and also the properties of the allyl and some substituted allyl cations, using the silver perchlorate technique.

Allyl phenyl ether was converted smoothly and in high yield into *p*-allyloxyacetophenone under all the conditions previously used: the reaction occurred to some extent even in benzene as the solvent:

$$CH_2{:}CH{\cdot}CH_2{\cdot}OPh + Ac^+ \longrightarrow p\text{-}CH_2{:}CH{\cdot}CH_2{\cdot}O{\cdot}C_6H_4{\cdot}COMe + H^+$$

In one or two experiments we did observe the formation of very small amounts of phenyl acetate which must have arisen as follows:

$$CH_2{:}CH{\cdot}CH_2{\cdot}\overset{+}{O}PhAc \longrightarrow PhOAc + CH_2{:}CH{\cdot}CH_2^+$$

It was apparent that under comparable conditions the allyl cation was not formed so readily as the benzyl cation. But-2-enyl (crotyl) and cinnamyl phenyl ethers behaved entirely differently giving, under all the conditions used, viscous and resinous products, respectively. The resinous materials from the cinnamyl ether were of variable composition but all appeared to contain a higher proportion of oxygen than the original ether, and the molecular weight (Rast) varied from 320 to 512. We have also found that these ethers usually produce similar polymeric products when treated with a little 70% perchloric acid in nitromethane although that from the cinnamyl ether had a higher carbon content but also a higher molecular weight (794). We were able to identify small amounts of phenol in some cases but the major portion of the products was non-phenolic. 1-Phenylallyl *p*-nitrobenzoate showed a similar behaviour towards 70% perchloric acid in nitromethane or acetic anhydride: fission was rapid and *p*-nitrobenzoic acid and polymeric material were produced. It would appear from the above results that fission of the ester, and also of the ethers, did occur but that the substituted allyl cation was unstable and "polymerised" in a manner analogous to that of the benzyl cation.

$$PhO{\cdot}CH_2{\cdot}CH{:}CHR \xrightarrow{H^+} Ph\overset{+}{O}H{\cdot}CH_2{\cdot}CH{:}CHR \longrightarrow PhOH + R{\cdot}CH{:}CH{\cdot}CH_2^+ \longleftrightarrow R{\cdot}\overset{+}{C}H{\cdot}CH{:}CH_2 \longrightarrow \text{"polymer"}$$

In view of the remarkable difference shown by allyl phenyl ether we decided to investigate the formation of the various allyl cations from silver perchlorate and the appropriate

* Part XI, *J.*, 1953, 986.

allyl halide. We again find that there is a marked difference between the unsubstituted allyl and the two γ-substituted allyl cations, although even with the allyl cation the formation of complex products often occurs especially when reactions are carried out in a medium of relatively high dielectric constant. Allyl perchlorate is hydrolysed by water to allyl alcohol and reacts with acetic anhydride forming allyl acetate; the yields of products were however not good. Resinous products were obtained from the perchlorate and *m*-xylene or mesitylene in nitromethane whilst benzene and anisole gave intractable black tars. But-2-enyl perchlorate was unstable and gave a black resin. Cinnamyl perchlorate in nitromethane in the absence of any other reactant gave resinous materials of variable composition and high molecular weight; the oxygen content of the unpurified resins was variable but persisted even when the cinnamyl perchlorate was prepared in an atmosphere of nitrogen, although the molecular weight of the product was reduced from about 860 to 430.

The products formed from anisole and phenol were approximately dimeric but the former contained methoxyl groups and the latter was phenolic, indicating that reaction had occurred. They showed only slight unsaturation towards potassium permanganate in aqueous acetone. The formation of the dimeric products may involve a cyclisation process of the type discussed by Baker, Haksar, McOmie, and Ulbricht (*J.*, 1952, 4310) but we find that allylmesitylene, in which there is no free *ortho*-position, is also converted by perchloric acid in nitromethane into a " polymeric " substance. It is also possible that addition of an allyl cation to the double linking of the allylic compound may occur.

The mode of " polymerisation " of the substituted allyl cations themselves may involve the loss of a proton to give a substituted allene which, under the influence of hydrogen ion, then polymerises. It is also possible that the incorporation of oxygen may result by simultaneous oxidation either by molecular oxygen or, more probably, by perchloric acid. The polymeric materials did not contain halogen.

In marked contrast to the results with the cinnamyl cation we find that the cinnamoyl cation closely resembles the more reactive aroyl cations previously investigated by Burton and Praill (*J.*, 1951, 529). Thus with anisole alone or in nitromethane or even benzene as a solvent we found that 91, 94, and 94% yields, respectively, of *p*-methoxyphenyl styryl ketone could be isolated when the reactions were carried out at 18—28°, 3°, and 18°, respectively, for similar times.

Experimental

Materials.—Silver perchlorate was dried as previously described (*J.*, 1950, 2036). Nitromethane, anisole, *m*-xylene, mesitylene, benzene, allyl bromide (b. p. 70—71°), and cinnamyl chloride (b. p. 115°/15 mm.) were all dried and redistilled. Acetic anhydride, acetyl chloride, and perchloric acid were " AnalaR " reagents. Cinnamyl bromide was prepared from the alcohol and hydrogen bromide in acetic acid and had m. p. 35°. But-2-enyl chloride, b. p. 81—83°, was fractionated from the mixture of chlorides obtained from crotyl alcohol and thionyl chloride.

p-*Allyloxyacetophenone.*—Allyl bromide (7·6 g.) was added to the spongy mass of yellow solid which was precipitated when potassium hydroxide (2·3 g.) in water (2·3 c.c.) was mixed with a solution of *p*-hydroxyacetophenone (4·8 g.) in dioxan (50 c.c.). After refluxing gently for 17 hr. the mixture was added to water and extracted twice with ether. The combined ethereal extracts were washed thrice with 2N-sodium hydroxide and then with water. The dried (Na_2SO_4) ethereal extract was evaporated, excess of dioxan being removed in a vacuum. The *ketone* (4·5 g.) distilled at 110—112°/0·5 mm. (Found: C, 75·3; H, 7·1. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%).

The 2 : 4-*dinitrophenylhydrazone* separated as red needles, m. p. 189°, from ethyl alcohol (Found: C, 57·2; H, 4·4; N, 15·6. $C_{17}H_{16}O_5N_4$ requires C, 57·3; H, 4·5; N, 15·7%).

Reaction of Allyl Phenyl Ether with Acetylium Perchlorate.—(a) *In nitromethane* Acetyl chloride (0·05 mole) in nitromethane (20 c.c.) was added during 15 min. to a cold (0—5°) solution of allyl phenyl ether (0·05 mole) and silver perchlorate (0·05 mole) in nitromethane (70 c.c.). After a further 45 min. at 0—5° the silver chloride was filtered off from the orange solution, the filtrate being allowed to fall on to crushed ice. Ethereal washings of the silver chloride were added to the filtrate and the combined extracts were washed with sodium hydrogen carbonate

solution and then with water until neutral. The residue obtained from the dried (Na_2SO_4) solution was distilled yielding fractions: (i) 0·3 g., b. p. 40—90°/0·5 mm., (ii) 8·0 g., b. p. 103—109°/0·5 mm. Fraction (i) was a mixture of unchanged allyl phenyl ether and phenyl acetate. The latter was identified by hydrolysis with boiling 2N-sodium hydroxide to phenol which was liberated by carbon dioxide (general procedure) and identified (standard procedure) as 2 : 4 : 6-tribromophenol, m. p. and mixed m. p. 90°. Fraction (ii) was *p*-allyloxyacetophenone, identified as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 188—189°.

(b) *In presence of acetic anhydride.* The experiment described under (a) was repeated but with acetic anhydride (0·05 mole) in the allyl phenyl ether–silver perchlorate–nitromethane solution. The red mixture was filtered after 30 min.; the ethereal extract showed a green fluorescence. Fractionation of the residue yielded: (i) 1·8 g., b. p. 120—122°/*ca.* 1 mm., (ii) 6·4 g., b. p. 116—118°/0·5 mm. Both fractions were *p*-allyloxyacetophenone; m. p.s and mixed m. p.s of the 2 : 4-dinitrophenylhydrazones, 188—189°.

(c) *In benzene.* The experiment described under (a) was repeated but with benzene (230 c.c.) instead of nitromethane as solvent. The acetyl chloride was also mixed with benzene (20 c.c.). The reaction was carried out at 8°. The orange solution was filtered after a further 30 min. The following fractions were obtained: (i) 0·8 g., b. p. 40—90°/0·5 mm., (ii) 1·0 g., b. p. 90—120° (mainly 116°)/0·5 mm., (iii) 0·7 g., b. p. 130—160°/0·5 mm., and a viscous residue (7 g.). Fraction (i) was a mixture of allyl phenyl ether and phenyl acetate. Fraction (ii) was *p*-allyloxyacetophenone, identified as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 188°.

Reaction of Allyl Phenyl Ether with a Small Amount of 70% Perchloric Acid in Acetic Anhydride.—Allyl phenyl ether (0·05 mole) in acetic anhydride (0·15 mole) was treated with two drops of 70% perchloric acid. The solution became red and the temperature rose from 15° to 40°. After 50 min. the solution was poured on to crushed ice and extracted twice with ether. The combined ethereal extracts were washed with sodium carbonate solution; a brown solid (0·3 g.), which gave an intensely fluorescent solution in ethyl alcohol, was then filtered off. The filtrate was then washed with water until neutral. The residue from the dried (Na_2SO_4) ethereal extract on fractionation yielded: (i) 2·2 g., b. p. 40—42°/0·5 mm., (ii) 0·5 g., b. p. 40—110°/0·5 mm., (iii) 2·8 g., b. p. 110—118°/0·5 mm. Fraction (i) redistilled at 178°/760 mm. and was allyl phenyl ether containing a very small amount of phenyl acetate. Fraction (iii) was *p*-allyloxyacetophenone, identified as the 2:4-dinitrophenylhydrazone, m. p. and mixed m. p. 187°.

Fission of Cinnamyl Phenyl Ether with Acetylium Perchlorate.—(a) *In nitromethane.* The ether (0·05 mole) was treated with silver perchlorate–acetyl chloride in nitromethane as described for allyl phenyl ether (above). After a further 40 min. the mixture was worked up in the usual way. A resin (9·2 g.) (Found: C, 73·1; H, 6·2%; *M*, 512) was obtained.

(b) *In presence of acetic anhydride.* The experiment was repeated but with acetic anhydride (0·05 mole) in the silver perchlorate–cinnamyl phenyl ether–nitromethane solution. The mixture was worked up after a further 30 min. The product was a brown resin (11 g.) (Found: C, 75·4; H, 6·2%; *M*, 349).

A similar resin (Found: C, 77·4; H, 8·9%; *M*, 320) was also obtained when the ether (0·025 mole) in acetic anhydride (0·2 mole) was treated with 2 drops of 70% perchloric acid. The mixture was kept for 50 min. before being worked up.

When but-2-enyl phenyl ether (0·05 mole) was treated as in (b) the product (9 g.) was a dark viscous oil from which phenyl acetate (2·7 g.), b. p. 80—84°/11 mm., was separated by fractional distillation.

Action of 70% Perchloric Acid on the Ethers in Nitromethane.—(a) *Allyl phenyl ether.* The ether (0·05 mole) in nitromethane (50 c.c.) was treated with 2 drops of 70% perchloric acid and the mixture heated on a steam-bath for 3 hr. The red solution was then cooled, poured into water, and extracted with ether. The ethereal extract was washed with sodium hydrogen carbonate solution and then with water until neutral. The residue after removal of solvent was separated into phenolic (3·1 g.) and non-phenolic (3·9 g.) portions by extracting its ethereal solution with 2N-sodium hydroxide. The phenolic portion was fractionated yielding: (i) 0·3 g., b. p. 90—110° (mainly 92°)/40 mm., and (ii) a viscous residue. Fraction (i) crystallised and was identified as phenol; the non-phenolic portion remained as a viscous gum.

(b) *Cinnamyl phenyl ether.* The addition of 2 drops of 70% perchloric acid to the ether (0·025 mole) in nitromethane (50 c.c.) produced an immediate deep red colour, and the temperature of the solution rose from 18° to 31°. The solution was left overnight and then heated on a steam-bath for 3 hr. On cooling the solution deposited a non-phenolic brownish red gum which dried to a " resin " (1·8 g.) in a vacuum-desiccator (Found: C, 82·6; H, 6·5%; *M*, 794). The mother-liquor was washed with sodium hydrogen carbonate solution, etc., and separated

into a phenolic portion (2·4 g.) (Found: C, 81·9; H, 7·3%; *M*, 324), and a non-phenolic portion (1·3 g.) (Found: C, 85·7; H, 8·0%; *M*, 467).

(c) *But-2-enyl phenyl ether.* The ether (0·05 mole) in nitromethane (50 c.c.) with 2 drops of 70% perchloric acid gave a golden yellow solution which darkened rapidly. After 4 hr. on a steam-bath the solution was poured into water, etc., and separated into phenolic (1·6 g.) and non-phenolic (3·7 g.) portions as described above. The latter remained as a viscous gum, whilst the phenolic portion gave on distillation phenol (0·5 g.), b. p. 80—82°/14 mm.

Fission of 1-*Phenylallyl* p-*Nitrobenzoate.*—(a) *In nitromethane.* The addition of 1 drop of 70% perchloric acid to a solution of 1-phenylallyl *p*-nitrobenzoate (1 g.) in nitromethane (10 c.c.) produced an immediate precipitate. This was filtered off and when recrystallised yielded *p*-nitrobenzoic acid, m. p. and mixed m. p. 234°, together with a little resinous material. The filtrate was diluted with ether, washed with aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). After removal of the solvents it yielded a "resin" (Found: C, 84·1; H, 6·8%; *M*, 840).

(b) *In acetic anhydride.* 1-Phenylallyl *p*-nitrobenzoate (1 g.) in acetic anhydride (10 c.c.) was treated with 1 drop of 70% perchloric acid. After 1 hr. the brown solution was added to cold water, extracted with ether, and separated into acidic and neutral portions with 2N-sodium hydroxide. The neutral portion (0·4 g.) was resinous (Found: C, 75·1; H, 6·8%; *M*, 383). The acidic portion was *p*-nitrobenzoic acid, m. p. and mixed m. p. 234°.

Reactions of Allyl Perchlorate.—(a) *In absence of other reactant.* Allyl bromide (0·05 mole) in nitromethane (20 c.c.) was added during 1 hr. to a cold (0—5°) solution of silver perchlorate (0·05 mole) in nitromethane; no gaseous product was evolved (manometer connected to apparatus) during this time or the next 90 min., after which the silver bromide was filtered off and the filtrate allowed to drop on to crushed ice. The filtrate was extracted with ether, and washed with sodium hydrogen carbonate solution, and then with water. The washings were combined with the aqueous layer, and the fraction that distilled below 98° was collected and added to the residue from the evaporated ethereal extract. The mixture with bromine yielded 2 : 3-dibromopropyl alcohol (4·2 g.), b. p. 212°, which was separated by distillation and identified by the m. p. (80°) of its phenylurethane.

(b) *With acetic anhydride.* Allyl bromide (0·05 mole) in acetic anhydride (20 c.c.) was added to a cold (0—5°) solution of silver perchlorate (0·05 mole) in acetic anhydride (20 c.c.) during 1 hr. After a further 70 min., the silver bromide was filtered off and the reaction product treated as above, except that sodium carbonate solution was used as the neutralising agent. On fractionation the residue (4·6 g.) gave: (i) 0·4 g., b. p. 94—102°, (ii) 2·3 g., b. p. 102—107° (mainly 104°), (iii) 0·7 g., b. p. 108—110°, and a black viscous residue (1 g.). Fraction (ii) was allyl acetate.

(c) *With* m-*xylene.* Silver perchlorate (0·05 mole) in *m*-xylene (0·05 mole) and nitromethane (70 c.c.) was treated during 1 hr. with allyl bromide (0·05 mole) in nitromethane (20 c.c.). After 2 hr. at 0—5° the silver halide was filtered off and the reaction product worked up in the usual way. A resinous product (Found: C, 87·4; H, 9·4%; *M*, 399) was obtained.

(d) *With mesitylene.* The experiment described under (c) was repeated with mesitylene (0·05 mole) in place of *m*-xylene. A "resin" (4 g.), insoluble in nitromethane, was obtained (Found: C, 86·8; H, 9·9%; *M*, 392). Viscous black tars were similarly obtained from benzene (0·75 mole) and anisole (0·05 mole).

"*But-2-enyl Perchlorate.*"—But-2-enyl chloride (0·05 mole) in nitromethane (25 c.c.) was added to a cooled (0—5°) solution of silver perchlorate (0·05 mole) in nitromethane (70 c.c.). After 45 min. the silver chloride was filtered off and the filtrate worked up in the usual way. A black resin insoluble in nitromethane (Found: C, 80·0; H, 10·4%; *M*, 433) was isolated.

"*Cinnamyl Perchlorate.*"—(*a*) Cinnamyl chloride (0·05 mole) in nitromethane (20 c.c.) was added during 30 min. to a cooled (0—5°) solution of silver perchlorate (0·05 mole) in nitromethane (75 c.c.). After a further hour the silver chloride was filtered off, the brown solution falling on to crushed ice; the silver halide was washed with ether. A yellow solid (2·4 g.), insoluble in both the ethereal and the aqueous layer separated; this was collected, washed with water and then with ether, and then dried (Found: C, 70·0; H, 5·6%; *M*, 865).

Repetition of the experiment in an atmosphere of dry nitrogen gave a buff resin (Found: C, 82·9; H, 6·7%; *M*, 428). The use of cinnamyl bromide as in (*a*) gave a yellow resin (Found: C, 84·9; H, 7·3%; *M*, 837).

(*b*) Repetition of experiment (*a*) but with cinnamyl bromide in presence of anisole (0·05 mole) and phenol (0·05 mole) gave an orange resin (Found: C, 82·4; H, 7·1; OMe, 11·2%; *M*, 438) and a sodium hydroxide-soluble orange resin (Found: C, 84·2; H, 6·7%; *M*, 330), respectively.

Allylmesitylene.—The Grignard reagent, from magnesium (4·9 g.) and bromomesitylene (40 g.) in ether (200 c.c.), and allyl bromide (24·2 g.) were refluxed for 6 hr. and then set aside overnight. Decomposition with ice and ammonium chloride gave a product which was repeatedly fractionated and finally distilled over sodium giving *allylmesitylene* (6·1 g.), b. p. 97—98°/10 mm. (Found : C, 89·8; H, 9·9. $C_{12}H_{16}$ requires C, 90·0; H, 10·0%).

When the hydrocarbon (1·5 g.) in nitromethane (10 c.c.) was treated with 1 drop of 70% perchloric acid the mixture darkened slowly and after a few hours tarry material separated.

Reaction of Cinnamoyl Perchlorate with Anisole.—The experiments, with silver perchlorate and anisole, were carried out as described in Part IV (*J.*, 1951, 529). The *p*-methoxyphenyl styryl ketone was identified by m. p. and mixed m. p. (107°).

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QUEEN ELIZABETH COLLEGE (UNIVERSITY OF LONDON), W.8. [*Received, January 21st,* 1954.]

Wool Wax. Part VI. The Synthesis and Stereochemistry of the Straight-chain α-Hydroxy-acids.*

By D. H. S. HORN and MISS Y. Y. PRETORIUS.

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A series of optically active straight-chain α-hydroxy-acids of known configuration has been synthesised from an optically active half-ester of (−)-malic acid by anodic coupling with aliphatic acids. The naturally occurring α-hydroxy-acids of wool wax and the derived 1 : 2-diols, phrenosinic (cerebronic) acid, and the 2-hydroxypentadecanoic acid from ustilic acids are assigned the D$_s$-configuration.

CONFIGURATIONAL correlation of optically active α-hydroxy-acids is unusually difficult, partly because higher homologues cannot be derived from lower ones by applying conventional methods of chain building to the carboxyl group, and partly because other chemical methods, which have been used for the correlation of the lower homologues (Levene *et al.*, *J. Biol. Chem.*, 1927, **71**, 465; 1928, **77**, 555), would be very laborious with higher homologues. For these reasons, only lactic acid, 2-hydroxybutanoic acid,† and 2-hydroxypentanoic acid have been directly correlated with glyceraldehyde, the stereochemical reference standard. However, Lemieux (*Canad. J. Chem.*, 1953, **31**, 396) has attempted a correlation of several naturally occurring higher α-hydroxy-acids by comparing the rotations of these acids and some of their derivatives with those of the corresponding lower homologues; but a formal chemical correlation has yet to be made. Our interest in the α-hydroxy-acids of wool wax (Horn, Hougen, and von Rudloff, *Chem. and Ind.*, 1953, 106, and Part V *) has led us to devise a simple synthetical method to accomplish this.

An optically active form of the monoethyl ester of acetylmalic acid has been used to obtain optically active 2-hydroxybutanoic, 2-hydroxyhexanoic, 2-hydroxyoctanoic, 2-hydroxydecanoic, and 2-hydroxyhexadecanoic acid by anodic coupling with the appropriate normal carboxylic acids in the following manner :

$$\begin{matrix} EtO_2C\cdot CH(OAc)\cdot CH_2\cdot CO_2H \\ + \\ R\cdot CO_2H \end{matrix} \xrightarrow[\text{and hydrolysis}]{\text{Anodic coupling}} HO_2C\cdot CH(OH)\cdot CH_2R$$

The required malic ester has been conveniently prepared by the reactions :

$$HO_2C\cdot CH(OH)\cdot CH_2\cdot CO_2H \xrightarrow{AcOCl} \begin{matrix} CH(OAc)\cdot CH_2 \\ | \quad\quad | \\ CO—O—CO \end{matrix} \xrightarrow{EtOH} \begin{matrix} EtO_2C\cdot CH(OAc)\cdot CH_2\cdot CO_2H \quad (I) \\ \text{and} \\ HO_2C\cdot CH(OAc)\cdot CH_2\cdot CO_2Et \quad (II) \end{matrix}$$

Although the product is a mixture of two isomers (I) and (II), it is not necessary to isolate the required acid (I), because its isomer (II), which has an α-substituent, does not undergo

* Part V, *J.*, 1954, 177. † Geneva numbering, CO_2H = 1.

anodic coupling. The properties of the acids synthesised in this manner from the naturally occurring (−)-malic acid (lævorotatory in dilute aqueous solutions) are summarised in section A of the Table.

A comparison of the properties of the naturally occurring α-hydroxy-acids, summarised in section C of the Table, with those synthesised from (−)-malic acid, clearly shows that they belong to the enantiomorphous series, which would be obtained from (+)-malic acid. Thus the 2-hydroxyhexadecanoic acid obtained from (−)-malic acid on admixture in exactly equal proportions with the 2-hydroxyhexadecanoic acid from wool wax was identical with a (±)-mixture synthesised from (±)-malic acid.

In section B of the Table, the properties of (+)-2-hydroxybutanoic acid and (+)-2-hydroxypentanoic acid are compared with those of (+)-lactic acid, with which they have been correlated chemically by Levene and his co-workers (*loc. cit.*). The dextrorotatory 2-hydroxy-butanoic and -pentanoic acids, as shown, are reported by Levene to yield lævorotatory sodium salts. On the other hand, the lævorotatory 2-hydroxybutanoic acid obtained by us from (−)-malic acid was found to yield, unexpectedly, a lævorotatory sodium salt. However, Levene did not measure the rotations of the pure acids in water, as we have done; he liberated the acids from their barium salts with an excess of hydro-

		$[\alpha]_D$ of acid				$[\alpha]_D$ of Na salt		$[\alpha]_D$ of Me ester	
R in (I)	M. p.	H_2O	Aq. HCl	EtOH	$CHCl_3$	H_2O	50% EtOH	Homog.	$CHCl_3$
Section A									
C_2H_5 ...	52·7—53·5°	−3·0°	+1·2°	−4·4°	+6·4°	−13·2°	—	—	—
C_4H_9 ...	61·0—61·6	−1·6	+1·3	−1·5	+5·6	−14·1	—	—	—
C_8H_{13} ...	70·2—70·6	+3	—	+1·5	+6·2	−10·3	−18°	+2·8°	+11°
C_8H_{17}	77·6—78·0	—	—	+1·6	+5·3	—	−15	+3·0	—
$C_{14}H_{29}$...	93·3—93·6	—	—	+1	+2·7	—	−15	—	—
Section B									
CH_3 ...	—	+2·67—+3·8 [a]	—	—	—	−10·5 [b]	—	−8·22 [c] *	—
C_2H_5 ...	55·0—55·5	−2·5 [d]	+2·3 [e]	−3·8 [d]	+6·8 [d]	− 8·7 [f]	—	−3·83 [e] *	—
C_3H_7 ...	—	—	+1·4 [f]	—	—	− 2·7 [f]	−20·7 [g]	−5·1 [h] *	+16 [h]
Section C									
$C_{12}H_{25}$ [i]	88·2—88·5	—	—	—	−3·1	—	—	—	−3·6
$C_{14}H_{29}$ [j]	93·3—93·5	—	—	−1	−3·2 [j]	—	+16	—	−3·6
$C_{24}H_{49}$...	100·5—101 [k]	—	—	—	—	—	—	—	—
	102·3—102·6 [m]	—	—	—	−1·76	—	—	—	—
$C_{13}H_{27}$ [g]	89·5—90·0	—	—	−2·1	—	—	+ 4·2	—	—

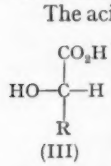
* Et ester.

[a] Jungfleisch and Godchot, *Compt. rend.*, 1905, **140**, 720. [b] Levene and Kuna, *J. Biol. Chem.*, 1941, **141**, 391. [c] Patterson and Lawson, *J.*, 1929, 2047. [d] Fredga, Tenow, and Billström, *Arkiv Kemi, Min., Geol.*, 1943, **16**, *A*, No. 21. [e] Levene and Haller, *J. Biol. Chem.*, 1927, **74**, 343. [f] Levene, Mori, and Mikeska, *ibid.*, 1927, **75**, 337. [g] Lemieux, *Canad. J. Chem.*, 1953, **31**, 396. [h] α_D for homogeneous value; *idem, ibid.*, 1951, **29**, 681. [i] Part V, *loc. cit.* [j] +3·6° in pyridine. [k] Klenk and Clarenz, *Z. physiol. Chem.*, 1939, **257**, 268. [l] *Idem, ibid.*, 1928, **174**, 221; $[\alpha]_D$ of acid +3·41° in pyridine. [m] Chibnall, Piper, and Williams, *Biochem. J.*, 1936, **30**, 100; $[\alpha]_D$ of acid +3·33° in pyridine.

chloric acid and measured the rotations of the resulting solution directly. When our acid was examined under these conditions, it was also dextrorotatory (see section A of the Table). When the solution was diluted with water and the rotation measured in a longer tube, it became lævorotatory (cf. Fredga, Tenow, and Billström, *Arkiv Kemi, Min., Geol.*, **1943**, **16**, *A*, No. 21). Similar effects of concentration, pH, and salts on the sign of rotation are well known (Stubbs, *J.*, 1911, **99**, 2268). It is clear then, that the lævorotatory 2-hydroxybutanoic acid from (−)-malic acid is the same as Levene's acid, which he erroneously reported to be dextrorotatory. While this observation does not alter the configurational correlation of (−)-sodium lactate with (−)-sodium 2-hydroxybutanoate, it becomes necessary to recognise (+)-lactic acid to have the same configuration as (−)-2-hydroxybutanoic acid, provided that Levene's chemical correlation is valid; and it almost certainly is valid, since our correlation of (−)-2-hydroxybutanoic acid with (−)-malic acid, as will be seen later, offers confirmation of this step by another route. Also this observation does not affect Levene's rule (*J. Biol. Chem.*, 1927, **75**, 337) that α-hydroxy-

acids with the configuration of L(+)-lactic acid show a shift in the rotation towards the left on passing from the free acids into their salts, and conversely; and, as is shown in the Table, this rule is now extended to the higher homologues, where the rotations of the free acids, measured in ethanol, are compared with those of their sodium salts in 50% ethanol.

The acids prepared by our method from (−)-malic acid have the configuration (III; R = alkyl) and, by analogy with the amino-acid convention, can be denoted as L$_s$ (Rosanoff, *J. Amer. Chem. Soc.*, 1906, **28**, 114; Wolfrom, Lemieux, Olin, and Weisblat, *ibid.*, 1949, **71**, 4057; cf. I.U.P.A.C. rules, *J.*, 1951, 3522).*


(III)

In conformity with the above proposals, the straight-chain α-hydroxy-acids of wool wax; the 1 : 2-diols of wool wax, which may be obtained from them by reduction with lithium aluminium hydride (Part IV, *J.*, 1953, 3533); phrenosinic (cerebronic) acid of brain (the stereoisomer of 2-hydroxytetracosanoic acid dextrorotatory in pyridine, Chibnall *et al.*, *Biochem. J.*, 1936, **30**, 100); and the 2-hydroxy-pentadecanoic acid obtained from ustilic acids (Lemieux, *loc. cit.*) are assigned the D$_s$-configuration. Although the chemical correlations made here confirm the indirect correlations of Lemieux, this correlation is partly fortuitous because, in passing up the homologous series from D$_s$-(−)-lactic acid to the naturally occurring 2-D$_s$-(−)-hydroxyhecadecanoic acid, there are two changes of sign (cf. Table); the first occurs as one passes from lactic acid to 2-hydroxypropionic acid, and the second, predicted on theoretical grounds (Levene, *J. Biol. Chem.*, 1928, **79**, 475) and confirmed by us, between 2-hydroxyhexanoic acid and 2-hydroxyoctanoic acid.

Since this paper was submitted for publication, a paper by Serck-Hanssen, Ställberg-Stenhagen, and Stenhagen (*Arkiv Kemi*, 1953, **5**, 203) has come to our notice. In it the possibility of synthesising long-chain optically active hydroxy-acids from smaller optically active acids by the anodic coupling method is suggested. It seems appropriate to record that we have extended our synthesis to unsaturated hydroxy-acids and have prepared, for example, 2-D$_s$-hydroxy-*cis*-tetracos-15-enoic acid (2-hydroxynervonic acid) from (+)-malic acid and erucic acid.

Experimental

Ethyl Hydrogen 2-L$_s$-*Acetoxysuccinates.*—Pure L$_s$-(−)-malic acid (naturally occurring form lævorotatory in dilute aqueous solutions) (25 g.) was obtained commercially or prepared by resolution with cinchonine (Dakin, *J. Biol. Chem.*, 1924, **59**, 9); the cinchonine (−)-malate formed was recrystallised at least 3 times; this is necessary if a purity of greater than 98% (−)-malic is required. The yield, based on the (±)-malic acid used, was *ca.* 10%. The acid was heated with acetyl chloride (75 c.c.) for 3 hr. The excess of chloride was removed at reduced pressure on a water-bath. To the residue was added dry ethanol (12 c.c.), and the mixture was heated for ½ hr. at 50°. Ethyl acetate (2 c.c.) was added and the crystal mass, which formed on cooling, was filtered off (23 g. or 60%). The *half-ester* crystallised from ethyl acetate in colourless needles, m. p. 50—51°, $[\alpha]_D^{29}$ −29·1° (*l*, 0·5; *c*, 10·5 in EtOH) (Found: C, 47·0; H, 6·0; Ac, 20·9%; equiv., 203. $C_8H_{12}O_6$ requires C, 47·1; H, 5·9; Ac, 21·1%; equiv., 204).

Ethyl Hydrogen DL-2-*Acetoxysuccinates.*—This mixture was prepared from (±)-malic acid as described above for the optically active forms. It crystallised from ethyl acetate in needles, m. p. 70·4—71·2° (Found: C, 47·3; H, 6·1; Ac, 21·2%; equiv., 203).

2-L$_s$-*Hydroxybutanoic Acid.*—Mixed ethyl hydrogen L$_s$-2-acetoxysuccinates (10 g.; the same amount was used in all subsequent electrolyses) were dissolved in methanol (80 c.c.) containing sodium (0·1 g.). Acetic acid (10 c.c.) was added and the mixture electrolysed in a cell containing a stainless-steel cooling-coil and two platinum-foil electrodes (25 × 35 cm.) reinforced with platinum wire (0·5 mm. diam.) and set 2 mm. apart. A current of about 1 amp. at about 50 v was passed until the mixture became neutral (10—15 hr.). The temperature in the vicinity of the plates was not allowed to exceed 35°. Sufficient water was added to make a 50% (v/v) alcoholic solution and the mixture was extracted with hexane. The hexane extract was washed with a dilute solution of potassium hydrogen carbonate and the hexane distilled off. The remaining *ethyl* L$_s$-2-*acetoxybutanoate* (5·1 g.) was distilled and the fraction of b. p. 92°/21 mm. retained (3·2 g.). It was refluxed for 30 min. with potassium hydroxide (3·2 g.) in water (40 c.c.).

* The Cahn–Ingold sequence rule (*J.*, 1951, 621) and Klyne's proposals (*Chem. and Ind.*, 1951, 1022) both lead to the prefix L.

To the cooled solution sufficient N-hydrochloric acid was added to neutralise 95% of the potassium hydroxide used. The solution was continuously extracted with ether for 2 hr. The ethereal extract was dried (Na_2SO_4) and evaporated, to yield L-2-*hydroxybutanoic acid* (1·5 g.). Volatile impurities were removed by steam-distillation. The acid crystallised from carbon tetrachloride–hexane in needles, m. p. 52·7—53·5° (Found: C, 46·4; H, 7·8%; equiv., 105. $C_4H_8O_3$ requires C, 46·1; H, 7·7%; equiv., 104), $[\alpha]_D^{16}$ −3·0° (*l*, 1; *c*, 6·19 in H_2O), $[\alpha]_D^{16}$ +6·4° (*l*, 0·5; *c*, 11·03 in $CHCl_3$), $[\alpha]_D^{16}$ −4·4° (*l*, 0·5; *c*, 8·53 in EtOH). Fredga *et al.* (*loc. cit.*) record m. p. 55·0—55·5°, $[\alpha]_D^{25}$ −2·5° (*l*, 2; *c*, 2·24 in H_2O), $[\alpha]_D^{25}$ −3·8° (*l*, 2; *c*, 2·15 in EtOH), and $[\alpha]_D^{25}$ +6·8° (*l*, 2; *c*, 2·48 in $CHCl_3$).

Determination of the Specific Rotation in the Manner described by Levene and Haller (J. Biol. Chem., 1927, **74**, 346).—L-2-Hydroxybutanoic acid (233 mg.), barium hydroxide (175 mg.), and concentrated hydrochloric acid (0·25 c.c.) were dissolved in water (up to 2 c.c.): the solution had $[\alpha]_D^{16}$ +1·2° (*l*, 0·5; *c*, 11·7). Levene and Haller (*loc. cit.*) record $[\alpha]_D^{22}$ +2·3°. The solution was diluted with water (up to 9 c.c.) and the rotation again measured ($[\alpha]_D^{16}$ −1·5°).

Sodium L-2-*Hydroxybutanoate*.—A solution of the acid in water was exactly neutralised with sodium hydroxide; the rotation measured directly was $[\alpha]_D^{20}$ −13·2° (*l*, 1; *c*, 4·17). Levene *et al.* (*J. Biol. Chem.*, 1927, **75**, 337) record $[M]_D$ −9·6°, *i.e.*, $[\alpha]_D$ −8·7° in water (the temperature and concentration are not given).

L-2-*Hydroxyhexanoic Acid*.—This *acid* was prepared from pure butanoic acid (18 c.c.) as described for L-2-hydroxybutanoic acid. The product on distillation yielded ethyl L-2-*acetoxyhexanoate* (5·5 g.), b. p. 120—124°/27—28 mm. The acid was recovered and purified as before. It crystallised from *iso*propyl ether–hexane (1 : 5) in needles, m. p. 61·0—61·6°, $[\alpha]_D^{18}$ +5·6° (*l*, 1; *c*, 6·84 in $CHCl_3$), $[\alpha]_D^{18}$ −1·5° (*l*, 1; *c*, 6·76 in EtOH), $[\alpha]_D^{18}$ −1·6° (*l*, 1; *c*, 4·40 in H_2O) (Found: C, 54·7; H, 9·2%; equiv., 134. $C_6H_{12}O_3$ requires C, 54·5; H, 9·2%; equiv., 132). To the pure acid (200 mg.) was added concentrated hydrochloric acid (0·2 c.c.) in water (up to 2 c.c.): $[\alpha]_D^{18}$ +1·3°. The solution was diluted with water (up to 9 c.c.) and the rotation measured: $[\alpha]_D^{18}$ −1·5°.

Sodium L-2-hydroxyhexanoate, prepared in solution, had $[\alpha]_D^{18}$ −14·1° (*l*, 2; *c*, 3·55 in H_2O).

L-2-*Hydroxyoctanoic Acid*.—This *acid*, prepared as described above from hexanoic acid [9·6 g., purified by fractional distillation and crystallisation (cf. Coulson and Jones, *J. Soc. Chem. Ind.*, 1946, **65**, 169), had f. p. −4·6°, n_D^{20} 1·4162. Ralston ("Fatty Acids and Their Derivatives," John Wiley and Sons, New York, 1948, p. 20) records f. p. −3·9°, n_D^{20} 1·41635]. It crystallised from *iso*propyl ether in needles, m. p. 70·2—70·6° (2·8 g.) (*l*, 0·5; *c*, 9·05 in $CHCl_3$), $[\alpha]_D^{19}$ +1·5° (*l*, 0·5; *c*, 6·80 in EtOH), $[\alpha]_D^{19}$ +3° (*l*, 0·5; *c*, 4·27 in H_2O containing 10—15% of MeOH) (Found: C, 60·0; H, 10·2%; equiv., 160. $C_8H_{16}O_3$ requires C, 60·0; H, 10·1%; equiv., 160). $[\alpha]_D^{19}$ +6·2°.

Sodium L-2-hydroxyoctanoate, prepared in aqueous solution by titration with 0·185N-sodium hydroxide, had $[\alpha]_D^{19}$ −10·3° (*l*, 0·5; *c*, 10·10 in H_2O), $[\alpha]_D^{19}$ −18° (*l*, 0·5; *c*, 5·05 in 50% aq. EtOH).

Methyl L-2-*Hydroxyoctanoate*.—This ester was prepared from the acid with methanol and sulphuric acid; it was a colourless liquid, n_D^{18} 1·4342, d_4^{16} 0·9686, b. p. 118°/22 mm., $[\alpha]_D^{16}$ +2·80° (*l*, 0·5; homog.) and $[\alpha]_D^{16}$ +11° (*l*, 0·5; *c*, 10·03 in $CHCl_3$).

L-2-*Hydroxydecanoic Acid*.—This *acid* (2·5 g.) was prepared from pure octanoic acid [6·4 g.; prepared as before by fractional distillation and crystallisation (cf. Coulson and Jones, *loc. cit.*), f. p. 16·1°, $n_D^{25\cdot2}$ 1·4256. Ralston (*op. cit.*, p. 23) records f. p. 16·3°, n_D^{20} 1·4285]. It crystallised from *iso*propyl ether in fine needles, m. p. 77·6—78·0°, $[\alpha]_D^{24}$ +5·3° (*l*, 0·5; *c*, 8·6 in $CHCl_3$), $[\alpha]_D^{24}$ +1·6° (*l*, 0·5; *c*, 7·3 in EtOH) (Found: C, 63·9; H, 10·7%; equiv., 189. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7%; equiv., 188).

Sodium L-2-hydroxydecanoate, obtained in aqueous solution by titration with 0·185N-sodium hydroxide and diluted with ethanol to make a 50% mixture, had $[\alpha]_D^{24}$ −15° (*l*, 1; *c*, 1·48 in 50% aq. EtOH).

Methyl L-2-hydroxydecanoate, prepared in the usual way, was a colourless liquid, n_D^{25} 1·4371, b. p. 152—155°/22 mm., $[\alpha]_D^{22}$ +3·0° (*l*, 0·5; homog.).

DL-2-*Hydroxyhexadecanoic Acid*.—This *acid*, prepared in the usual manner from *n*-tetradecanoic acid [9·5 g.; prepared by fractionation of its methyl ester at 1 mm. in a spinning-band fractionation column, followed by crystallisation of the best distillates, m. p. 54·3—54·8°. Ralston (*op. cit.*, p. 32) records 54·5°]. The electrolysis product yielded the crude acid (2·3 g.), m. p. 80·5—82·8°. Twice recrystallised from methanol, it had m. p. 85·8—86·6° (Found: C, 70·7; H, 11·7%; equiv., 272. Calc. for $C_{16}H_{32}O_3$: C, 70·5; H, 11·8%; equiv., 272). A mixed m. p. with DL-2-hydroxyhexadecanoic acid (m. p. 86·0—86·5°; Part V) was 85·8—86·5°.

L$_s$-2-*Hydroxyhexadecanoic Acid.*—This *acid* was prepared as described for the DL-compound. Crystallised from methanol, and hexane, it had m. p. 93·3—93·6°, $[\alpha]_D^{26}$ +2·7° (*l*, 1; *c*, 1·98 in $CHCl_3$), $[\alpha]_D^{26}$ +1° (*l*, 0·5; *c*, 2·24 in EtOH) (Found: C, 70·3; H, 11·7%; equiv., 275. $C_{16}H_{32}O_3$ requires C, 70·5; H, 11·8%; equiv., 272). On admixture with an equal amount of D$_s$-2-hydroxyhexadecanoic acid (Part V) (m. p. 93·3—93·6°), the m. p. was 86·0—86·7°. The m. p. of this mixture on admixture with DL-2-hydroxyhexadecanoic acid was 86·0—86·6°.

A solution of sodium L$_s$-2-hydroxyhexadecanoate in 50% aqueous ethanol had $[\alpha]_D^{26}$ −15° (*l*, 1; *c*, 9·30).

D$_s$-2-*Hydroxyhexadecanoic Acid.*—The rotation of the acid described in Part V, measured in ethanol, was $[\alpha]_D^{22}$ +1° (*l*, 0·5; *c*, 7·3). Its sodium salt had $[\alpha]_D^{22}$ +16° (*l*, 1; *c*, 1·49 in 50% aq. EtOH).

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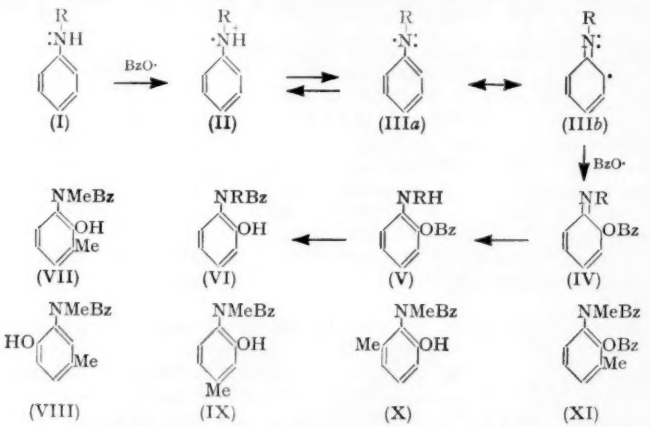
The Oxidation of N-*Alkylanilines and Related Compounds with Benzoyl Peroxide.*

By JOHN T. EDWARD.

[Reprint Order No. 4758.]

Monoalkylamino-aromatic compounds are oxidized by benzoyl peroxide to *o*-benzamidophenols.

BECAUSE of the widespread occurrence in Nature of *o*-aminophenolic compounds (*e.g.*, 3-hydroxyanthranilic acid, damascanene, vomicine), methods for their preparation by the direct oxidation of aromatic amines are of some interest. Gambarjan (*Ber.*, 1909, **42**, 4003) found that diphenylamine (I; R = Ph) was oxidized by benzoyl peroxide to *o*-*N*-phenylbenzamidophenol (VI; R = Ph) in 38% yield. The reaction is generally applicable to secondary aromatic amines, as shown by the results in Table 1. Yields are low, but the simplicity of the reaction and the ease of isolating the phenol will commend the method



in some instances. With most amines the reaction is complete in 10—15 minutes. However, *p*-chloro-*N*-methylaniline is oxidized more slowly, and *N*-methylanthranilic acid resists attack (cf. Horner and Scherf, *Annalen*, 1951, **573**, 35).

Except for *o*-*N*-methylbenzamidophenol (VI; R = Me) (Clark, *J.*, 1926, 232) and its ethyl analogue (VI; R = Et) (Anderson and Bell, *J.*, 1949, 2668), the phenols in Table 1 are new compounds. The structures (VI; R = Me, Et, and CH_2Ph) for the phenols from *N*-methyl-, *N*-ethyl-, and *N*-benzyl-aniline were proved by preparing these phenols also by the alkylation of 2-phenylbenzoxazole and hydrolysis of the benzoxazolonium salts (cf. Clark, *loc. cit.*). The phenols (VI; R = Pr^n and Bu^n) were obtained in small yield by the alkylation and subsequent benzoylation of *o*-aminophenol; the *o*-benzamidophenol also formed was converted into 2-phenylbenzoxazole by heating the product to 170°, the unchanged *o*-*N*-alkylbenzamidophenols being extracted from the cooled melt with alkali. They were identical with the phenols obtained by oxidizing (I; R = Pr^n and Bu^n). 1-Benzoyl-1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline was prepared by benzoylation of 1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline in sodium carbonate solution, and identified (m. p. and mixed m. p.) with the oxidation product of 1 : 2 : 3 : 4-tetrahydroquinoline.

The assumption that the other phenols are also *o*-benzamidophenols results in unambiguous structures for all of them except that obtained from *N*-methyl-*m*-toluidine, which could be (VII) or (VIII). The infra-red absorption spectrum of this compound (A)

TABLE 1. *Phenols from the oxidation of amines with benzoyl peroxide.*

Amine oxidized	Phenol	Yield, %	M. p.	Formula		C, %	H, %
N-Methylaniline	*o*-*N*-Methylbenzamidophenol	30	158—159° [a]	$C_{14}H_{13}O_2N$	Found	74·4	5·8
					Calc.	74·0	5·8
N-Ethylaniline	*o*-*N*-Ethylbenzamidophenol	37	160—162 [b]	$C_{15}C_{15}O_2N$	Found	74·6	6·2
					Calc.	74·6	6·2
N-Propylaniline	*o*-*N*-Propylbenzamidophenol	20	131—134	$C_{16}H_{17}O_2N$	Found	75·0	6·4
					Reqd.	75·3	6·7
N-Butylaniline	*o*-*N*-Butylbenzamidophenol	35	120—122	$C_{17}H_{19}O_2N$	Found	75·7	6·8
					Reqd.	75·8	7·1
N-*iso*Pentylaniline	*o*-*N*-*iso*Pentylbenzamidophenol	20	77—81	$C_{18}H_{21}O_2N$	Found	76·5	7·4
					Reqd.	76·3	7·5
N-Benzylaniline	*o*-*N*-Benzylbenzamidophenol	8	159—160	$C_{20}H_{17}O_2N$ [c]	Found	79·2	5·6
					Reqd.	79·1	5·7
N-Methyl-*o*-toluidine	3-Methyl-2-*N*-methylbenzamidophenol	8	152—155	$C_{15}H_{15}O_2N$	Found	74·3	6·1
					Reqd.	74·6	6·3
N-Methyl-*m*-toluidine	4-Methyl-2-*N*-methylbenzamidophenol	10	213—215	$C_{15}H_{15}O_2N$	Found	74·0	6·5
					Reqd.	74·6	6·3
N-Methyl-*p*-toluidine	5-Methyl-2-*N*-methylbenzamidophenol	31	189—193	$C_{15}H_{15}O_2N$	Found	74·3	6·2
					Reqd.	74·6	6·3
p-Chloro-*N*-methylaniline	5-Chloro-2-*N*-methylbenzamidophenol	19	210—211	$C_{14}H_{12}O_2NCl$	Found	64·5	4·4
					Reqd.	64·3	4·6
N-Ethyl-α-naphthylamine	1-*N*-Ethylbenzamido-2-naphthol	40	228—230	$C_{19}H_{17}O_2N$	Found	77·4	5·7
					Reqd.	78·3	5·9
1 : 2 : 3 : 4-Tetrahydroquinoline	1-Benzoyl-1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline	16	174—175	$C_{16}H_{15}O_2N$ [d]	Found	75·7	5·9
					Reqd.	75·9	6·0

[a] Clark (*loc. cit.*) reports m. p. 164°. [b] Anderson and Bell (*loc. cit.*) report m. p. 164°. [c] Found: N, 4·6. Required: N, 4·7%. [d] Found: N, 5·6. Required: N, 5·5%.

TABLE 2. *Infra-red absorption of some benzamidophenols.*

	1 : 2 : 4-Compounds			1 : 2 : 3-Compounds	
	Normal *	(IX)	A	Normal *	(X)
C–H out-of-plane deformation	810	807	806	770	(774, 778) †
" Ring-breathing " frequency	1000w	—	1003w	1010s	1008s
C–H in-plane deformation	1125	1128	1121	1095	1104

w = weak, s = strong.

* Whiffen and Thompson, *J.*, 1945, 268; Whiffen, personal communication.

† The second band is probably due to the vibration (unknown) giving rise to a band at 785 $cm.^{-1}$ in (IX) and 781 $cm.^{-1}$ in A.

in a Nujol mull over the range 1300—670 $cm.^{-1}$ (Table 2) indicates that it is most probably a 1 : 2 : 4-trisubstituted benzene, and so favours (VIII); the spectra of the phenols (IX) from *N*-methyl-*p*-toluidine and (X) from *N*-methyl-*o*-toluidine are included for comparison. (For these measurements and their interpretation I am greatly indebted to Dr. D. H.

Whiffen.) The formula (VII) for the phenol from *N*-methyl-*m*-toluidine would, on the mechanism advanced below, require (XI) as an intermediate; and space-filling models show that the formation of this compound is extremely difficult because of steric hindrance.

The neutral products of the oxidations were usually intractable tars. Very small quantities of crystalline products could be separated by chromatography on alumina; the structure of these compounds is uncertain, and is being investigated further.

The work of Horner and his co-workers (*loc. cit.*; Horner and Schwenk, *Annalen*, 1950, **566**, 69; Horner and Betzel, *ibid.*, 1953, **579**, 175; Horner and Hubenett, *Ber.*, 1952, **85**, 804) indicates strongly that the first stage in the attack of benzoyl peroxide on an aromatic amine is the abstraction of one electron and the formation of an aminium ion-radical. In the case of secondary amines (I) the aminium ion (II) may lose a proton to the benzoate ion and form the conjugate base (III) which, like (II), exists as a resonance hydrid of which two canonical forms are shown. The subsequent steps (III*b* ⟶ IV ⟶ V ⟶ VI) all find ample analogy in the literature, the last stage being the ready *ortho*-O⟶N migration of an acyl group (Taylor and Baker, " Sidgwick's Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1945, p. 75). This mechanism is similar to that of Cosgrove and Waters (*J.*, 1949, 3189) for the oxidation of phenols by benzoyl peroxide.

Experimental

Formation of Phenols by Oxidation with Benzoyl Peroxide.—Benzoyl peroxide was crystallized by addition of methanol to a concentrated solution in chloroform, and dried thoroughly *in vacuo* at room temperature. It was added to an equimolar quantity of the amine dissolved in about 20 volumes of benzene and cooled in ice. After 20 min. (or overnight for *p*-chloro-*N*-methylaniline) the solution was extracted with dilute aqueous sodium hydroxide. The gummy solid obtained on acidification was washed with sodium hydrogen carbonate to remove benzoic acid, and then digested with a small quantity of aqueous methanol. The yield of crude phenol is recorded in Table 1; one or two recrystallizations from aqueous methanol (charcoal) afforded the pure phenol as colourless needles or rhombs.

The phenol from *N*-ethyl-α-naphthylamine crystallized directly from the reaction mixture in almost pure condition; extraction of the benzene solution with alkali removed only a very small additional quantity of impure product.

Equally good yields of phenols were obtained by conducting the oxidations in formamide or chloroform solution, but use of ethyl ether gave lower yields. The yield decreased when the molar ratio of amine to peroxide was greater or less than 1 : 1. Alteration of the temperature of the reaction had little effect.

The phenols, like *o*-benzamidophenol, gave no colour with aqueous ferric chloride or with anhydrous ferric chloride in chloroform–pyridine (cf. Soloway and Wilson, *Analyt. Chem.*, 1952, **34**, 979). They gave a feeble Millon reaction. In concentrated sulphuric acid, on addition of a drop of 40% aqueous formaldehyde, 1-*N*-ethylbenzamido-2-naphthol gave a blue colour fading to green, *o*-*N*-benzylbenzamidophenol gave a red, and 4-methyl-2-*N*-methylbenzamidophenol a pink colour. It was necessary to heat the mixture containing 3-methyl-2-*N*-methylbenzamidophenol (orange red) and the *o*-*N*-alkylbenzamidophenols (gold or sherry colours); even under these conditions 5-chloro-2-*N*-methylbenzamidophenol gave no colour.

Formation of Phenols from 2-*Phenylbenzoxazole.*—The benzoxazolium compounds were prepared by refluxing a solution of 2-phenylbenzoxazole with an alkylating agent (methyl sulphate in benzene for 7 hr.; ethyl sulphate in xylene for 3 hr.; benzyl bromide in dimethylformamide for 5 hr.). The cooled solution was treated with aqueous alkali, the aqueous solution was extracted with benzene to remove neutral materials, and the *o*-benzamidophenols (VI; R = Me, Et, and CH_2Ph) were precipitated by acidification. These were identical (m. p. and mixed m. p.) with those from the oxidation of (I; R = Me, Et, and CH_2Ph). The m. p.s of R = Me and Et) are lower than those reported in the literature, but are very greatly affected by the rate of heating.

Formation of Phenols from o-*Aminophenol.*—*n*-Propyl bromide (2 c.c.) and *o*-aminophenol (2 g.) were heated in ethanol (15 c.c.) under reflux for 4 hr. The residue after removal of the ethanol was benzoylated in aqueous sodium carbonate and the phenols were extracted with benzene. They were then transferred to aqueous alkali, and the mixed benzamidophenols (m. p. *ca.* 100°) precipitated by making the solution strongly acidic. This material was heated to 170° for 10 min.; unchanged *o*-*N*-propylbenzamidophenol was extracted from the cooled

melt with alkali, and crystallized from aqueous methanol as clear cubes. It was identical (m. p. and mixed m. p.) with the phenol from the oxidation of (I; R = Pr^n). In the same way (VI; R = Bu^n) was prepared and proved identical with the oxidation product of (I; R = Bu^n).

This work was commenced under the supervision of Sir Robert Robinson, F.R.S., O.M., to whom I am grateful for his continued interest and encouragement. I wish also to thank the Royal Commission for the Exhibition of 1851 for a Science Scholarship, the University of Birmingham for an I.C.I. Research Fellowship, and Professor M. Stacey, F.R.S., and Professor W. Cocker for advice and encouragement and for facilities to complete this work.

DYSON PERRINS LABORATORY, SOUTH PARKS ROAD, OXFORD.
CHEMISTRY DEPARTMENT, THE UNIVERSITY, BIRMINGHAM, 15. [*Received, October 29th,* 1953.]

Mesomorphism and Chemical Constitution. Part II. The* trans-p-n-*Alkoxycinnamic Acids.*

By G. W. GRAY and BRYNMOR JONES.

[Reprint Order No. 4908.]

Thirteen pure *trans-p-n*-alkoxycinnamic acids have been prepared, and their mesomorphic transition temperatures determined. The mesomorphic properties are compared with those exhibited by the 6-*n*-alkoxy-2-naphthoic acids. The variations from previously determined transition temperatures for these cinnamic acids are discussed.

COMPARISON of the mesomorphic properties of the 6-*n*-alkoxy-2-naphthoic acids (Part I *) with those of the *trans-p-n*-alkoxycinnamic acids (Bennett and Brynmor Jones, *J.*, 1939, 420) reveals differences not to be expected in compounds which display such similarity of constitution. Unlike the naphthoic acids, the series of cinnamic acids shows no regularity of the upper transition points, or of smectic–nematic, and smectic–isotropic transition points. Moreover, hexadecyloxycinnamic acid exhibits a nematic phase, whilst the corresponding naphthoic acid is purely smectic. The only similarities between the two series would seem to be that all the ethers examined, from methyl upwards, exhibit mesomorphism, and that smectic properties are introduced, with a monotropic phase, in the nonyl ethers. The octadecyloxycinnamic acid was not examined by Bennett and Brynmor Jones (*loc. cit.*), but this has now been done in order to make the series of cinnamic acids comparable with the series of naphthoic acids. This acid melts at 120·5° to a smectic state, which changes to the isotropic liquid at 157·5°, without showing any nematic phase. When these values were added to a graph of the recorded constants for the cinnamic acids, they seemed misplaced in relation to the lower members. The series of *trans-p-n*-alkoxycinnamic acids (methyl—decyl, dodecyl, hexadecyl, and octadecyl) was therefore prepared afresh, and the transition points redetermined in the electrically heated block recently described (Gray, *Nature*, 1953, **172**, 1137). The new values for the transitions (solid–nematic or smectic, smectic–nematic, and smectic or nematic–isotropic) are tabulated on p. 1468.

When these values are plotted against the number of carbon atoms in the alkyl chain, the transition temperatures exhibit regularities similar to those already reported for the *p-n*-alkoxybenzoic acids (Gray and Brynmor Jones, *J.*, 1953, 4179) and the 6-*n*-alkoxy-2-naphthoic acids (Part I, *J.*, 1954, 683). The upper transition points now lie on two smooth curves, the upper representing the ethers with an even number, and the lower curve those with an uneven number, of carbon atoms in the alkyl group. These curves fall gradually, and are joined by the rising curve which passes through the smectic–nematic and smectic–isotropic transition points of the nonyl, decyl, dodecyl, hexadecyl, and octadecyl ethers. Like the analogous ethers of the benzoic and naphthoic acids, the hexadecyl and octadecyl ethers are purely smectic, as proved by their appearance from the isotropic state in bâtonnets. Thus, the resemblance between the alkoxycinnamic acids and the 6-*n*-alkoxy-2-naphthoic acids is very close. Both series show a regularity of the transition points, with smectic

* Part I, *J.*, 1954, 683.

phases appearing at the nonyl ether. There is, moreover, a general decrease in the stability of the mesophases with increasing chain length, and an increasing stability of the smectic phases with increasing molecule length up to the hexadecyl ether; thereafter there is a slight decrease to the upper transition point of the octadecyl ether. The

Alkyl group	Temp. of transition to			Phase length of	
	smectic	nematic	isotropic	smectic	nematic
Methyl	—	173·5°	190°	—	16·5°
Ethyl	—	194	198·5	—	4·5
Propyl	—	167	184·5	—	17·5
Butyl	—	156	189·5	—	33·5
Pentyl	—	139·5	179·5	—	40
Hexyl	—	153	181·5	—	28·5
Heptyl	—	148	175	—	27
Octyl	—	146	174·5	—	28·5
Nonyl	138·5°	144	171	5·5°	27
Decyl	136	150·5	169	14·5	18·5
Dodecyl	132	157	165	25	8
Hexadecyl	118	—	159	41	—
Octadecyl	120·5	—	157·5	37	—

qualitative agreement between the two series would have been complete had the smectic phase of nonyloxycinnamic acid been monotropic, as reported earlier. However, repeated preparation and purification of this compound gave in all cases the constants now quoted, with an enantiotropic smectic phase of length 5·5°.

In their principal characteristics, the agreement between the two series is good. It was, of course, not to be expected that the similarity would be any closer, and that, for instance, the phase lengths of analogous ethers would be identical or that the maximum phase lengths would occur at the same point in each series. The naphthoic acids should have higher m. p.s than the cinnamic acids. This in fact is the case in nine of the thirteen ethers, but probably varying factors affect the m. p. It is even more significant that in all cases the upper transition points of the naphthoic acids are higher than those of the cinnamic acids. Therefore, the mesophases of the former are more stable. The average upper transition temperature for the naphthoic acids is 192·1°, and for the cinnamic acids 176·5°—a difference of 15·6°. The smectic–nematic and smectic–isotropic transition temperatures are much closer, and are higher in the naphthoic acids in only three of the five cases. The average value for the naphthoic acids (153°) is indeed less by 0·6° than the average of 153·6° for the cinnamic acids. It is possible, therefore, that the naphthalene system gives rise to a greater overall thermal stability of the mesophases, but that, relative to the nematic phases, the smectic phases of the latter are, on the average, slightly more stable.

The order of mesomorphic stability for three series of acids is as shown below, where the figures represent the average fall in the upper transition points.

6-*n*-Alkoxy-2-naphthoic acids $\xrightarrow{15{\cdot}6°}$ *trans*-*p*-*n*-Alkoxycinnamic acids $\xrightarrow{31{\cdot}4°}$ *p*-*n*-Alkoxybenzoic acids

Decreasing thermal stability of the mesophases →

It is noteworthy that these decreases are accompanied by a decrease in the number of double bonds in the system, and further evidence is forthcoming to verify this.

The above values vary substantially from those obtained by Bennett and Brynmor Jones (*loc. cit.*), and there may be a number of contributory reasons for the differences. When the earlier measurements were made, the higher alkyl halides (especially $C_7H_{15}X$ to $C_{12}H_{25}X$) were not readily obtained pure and, although the analyses for the corresponding alkoxycinnamic acids were satisfactory, the acids may not have been free from isomers. However, in addition, these compounds are sensitive to sunlight and heat, and when some of the original samples, prepared some 15 years ago, were re-examined there was in many cases almost a complete loss of mesomorphic characteristics. For example, the nonyl ether, reported to have m. p. 141° and upper transition point 163°, melted to the isotropic liquid over the range 137—141°. Samples of the acids prepared afresh for this investigation

showed reduced mesomorphic properties when set aside—the rapid deterioration in sunlight points to isomerisation. When octadecyloxycinnamic acid was exposed to sunlight during 3 months, the original constants of 120·5° and 158° fell to 117° and 151—154°. The last transition was so indefinite that, had it not been previously known that the sample was purely smectic, the presence of a short nematic phase between 151° and 154° would have been suspected. Such behaviour may account for the reported observation of a short nematic phase in the hexadecyl ether.

These compounds are also affected by heat, as shown by the behaviour of the nonyl ether. This was heated in an oil-bath at 160° for 1 hour, the nematic melt was cooled, and the m. p. determined. The material softened at 126°, and flowed at 136° to a turbid melt, which cleared at 157—164°. The constants of the pure acid are 138·5°, 144°, and 171°. Moreover, after this treatment no definite smectic phase was detectable on cooling the isotropic liquid on a slide. This confirms the earlier report of a monotropic smectic phase in this compound.

To minimise these risks in the present investigation, a fresh slide was mounted for the determination of each transition point, and no sample was exposed to light or high temperatures for more than 2—3 minutes.

No difference was found in the enantiotropic polymorphic transition of the hexyloxycinnamic acid, or in the textures of the mesophases reported by Bennett and Brynmor Jones.

The *trans-p-n*-alkoxycinnamic acids were prepared by condensing the *p-n*-alkoxybenzaldehydes with malonic acid in pyridine (piperidine as catalyst). This method is more satisfactory than the homologous alkylation of *trans-p*-hydroxycinnamic acid (Bennett and Brynmor Jones, *loc. cit.*). For example, the octadecyl ether was prepared by both of these methods. The constants, 120·5° and 157·5°, for the acid prepared by the former method were obtained after only two crystallisations from glacial acetic acid, whereas they were obtained for the material prepared by the second method only after seven crystallisations—two from glacial acetic acid, three from benzene, and two from absolute ethyl alcohol. More readily purified compounds are therefore obtained by the condensation method.

Experimental

Determination of the Mesomorphic and Polymorphic Transition Temperatures.—The approximate transitions for solid–nematic and smectic, smectic–nematic, and smectic and nematic–isotropic were first determined in a wide m. p. capillary tube in a well-stirred paraffin bath. The electrically heated block (Gray, *loc. cit.*) was raised to within 5° of each value, and a thin section of the acid, obtained by melting between a glass slide and a cover slip, inserted in the slide slot. The temperature was then raised at less than 2°/min. until each transition had occurred. A fresh slide was mounted for each transition, and no specimen was exposed to light or heat for more than 2—3 min. The corrected values obtained are tabulated above.

Preparation of Materials.—p-n-*Alkoxybenzaldehydes.* *p*-Hydroxybenzaldehyde (12·2 g., 0·1 mol.), anhydrous potassium carbonate (60 g., 0·4 mol.), *cyclo*hexanone (80 ml.), and the *n*-alkyl bromide or iodide (0·16 mol.) were refluxed and agitated vigorously. Alkylation was complete after 1—3 hr., the mixture then being pale yellow or colourless. The solution was decanted from the potassium carbonate, which was washed with ether. The washings were

Table 1.

Alkyl group	B. p.	Found, % C	Found, % H	Formula	Required, % C	Required, % H
Et	106°/3 mm.	71·9	6·5	$C_9H_{10}O_2$	72·0	6·7
Pr	144°/14 mm.	73·3	7·4	$C_{10}H_{12}O_2$	73·2	7·3
$C_{10}H_{21}$	185°/4 mm.	77·9	10·0	$C_{17}H_{26}O_2$	77·85	9·9
$C_{15}H_{25}$	194°/8 mm.	78·6	10·4	$C_{19}H_{30}O_2$	78·6	10·4
$C_{16}H_{33}$	230°/3 mm.	79·9	10·9	$C_{23}H_{38}O_2$	79·8	11·0
$C_{18}H_{37}$	240°/2 mm.	80·2	11·2	$C_{25}H_{42}O_2$	80·2	11·2

added to the *cyclo*hexanone extract, and both solvents distilled off on the water-bath under reduced pressure. The residual *p-n*-alkoxybenzaldehydes were then distilled under reduced pressure, and obtained as colourless liquids or low-melting solids (65—75% yield). The yields of the hexadecyl and octadecyl ethers were never more than 60%—their high b. p.s resulted in

charring during distillation. The butyl to nonyl ethers have been prepared, and their b. p.s recorded, by Weygand and Gabler (*J. pr. Chem.*, 1940, **155**, 332). Table 1 gives the b. p.s and analyses for the remainder of the series. The dodecyl, hexadecyl, and octadecyl aldehydes are waxy solids of m. p.s 24°, 34°, and 48·5° respectively.

trans-p-n-*Alkoxycinnamic acids.* The *p-n*-alkoxybenzaldehyde (0·02 mol.), malonic acid (3·2 g., 0·04 mol.), pyridine (8 ml.), and piperidine (3 drops) were heated at 100° for 3 hr. The mixture was poured on ice (25 g.) and concentrated hydrochloric acid (25 ml.). The precipitate was collected, washed with dilute hydrochloric acid and water, and crystallised from 98% acetic acid. The yields of the colourless products were 90—100% and, after a total of three crystallisations from 98% acetic acid, the m. p.s were constant. The analyses for these acids are in Table 2.

TABLE 2.

Alkyl group	Found, % C	Found, % H	Formula	Required, % C	Required, % H	Alkyl group	Found, % C	Found, % H	Formula	Required, % C	Required, % H
Me	67·3	5·5	$C_{10}H_{10}O_3$	67·4	5·6	C_8H_{17}	73·7	8·7	$C_{17}H_{24}O_3$	73·9	8·7
Et	68·7	6·3	$C_{11}H_{12}O_3$	68·8	6·25	C_9H_{19}	74·3	9·0	$C_{18}H_{26}O_3$	74·5	9·0
Pr	69·7	6·8	$C_{12}H_{14}O_3$	69·9	6·8	$C_{10}H_{21}$	74·8	9·2	$C_{19}H_{28}O_3$	75·0	9·2
Bu	70·9	7·2	$C_{13}H_{16}O_3$	70·9	7·3	$C_{12}H_{25}$	76·1	9·5	$C_{21}H_{32}O_3$	75·9	9·65
C_5H_{11} ...	71·9	7·7	$C_{14}H_{18}O_3$	71·8	7·7	$C_{16}H_{33}$	77·3	10·4	$C_{25}H_{40}O_3$	77·3	10·3
C_6H_{13} ...	72·6	8·1	$C_{15}H_{20}O_3$	72·6	8·1	$C_{18}H_{37}$	78·1	10·7	$C_{27}H_{44}O_3$	77·9	10·6
C_7H_{15} ...	73·3	8·5	$C_{16}H_{22}O_3$	73·3	8·4						

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Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part XIII. Some Alkylbenzoic Acids exhibiting Steric Effects.*

By J. F. J. DIPPY, S. R. C. HUGHES, and J. W. LAXTON.

[Reprint Order No. 4917.]

The thermodynamic dissociation constants of eleven alkylbenzoic acids have been determined conductimetrically (as well as those of 1- and 2-naphthoic acids). Nine of the benzoic acids possess substituents in the *ortho*-position, and the resultant enhancements of acid strength are capable of an interpretation in harmony with the theory of steric inhibition of mesomerism. Striking regularities in the increments in strength have been recorded for the introduction of methyl groups at the 2- and at the 6-positions of alkylbenzoic acids. The method employed for the determination of acid strengths is a refinement of that described in earlier parts of this series.

ALTHOUGH the literature contains the classical dissociation constants of a number of alkylbenzoic acids, the need has arisen for more dependable and extensive data for the strengths of these acids. The thermodynamic dissociation constants recorded here relate to benzoic acid substituted with (i) two or three methyl groups and, (ii) one higher alkyl group (ethyl, *iso*propyl or *tert.*-butyl) at the *ortho*-position. The strengths of 1- and 2-naphthoic acids have been redetermined.

Table 1 sets out the thermodynamic dissociation constants of these acids (in aqueous solution at 25°) and the values of $\Lambda_{0(\text{acid})}$. The methods of calculating these data from the conductivity measurements in acid and in sodium salt solution, respectively, were those described earlier in this series, although refinements in the experimental technique have been introduced. All dissociation constants previously recorded for the above acids are classical values, and these are shown in Table 1 with our values of the classical constants for comparison.

The anion mobilities (as given by Λ_0) are all remarkably consistent with molecular size,

* Two earlier papers (*J.*, 1941, 550; 1944, 411), which appeared under specific titles, are regarded as Parts XI and XII of this series.

as illustrated by the three *o*-alkylbenzoic acids (cf. Λ_0 for *o*-, *m*-, and *p*-toluic acids = 381·2, 379·3, and 397·7, respectively). The naphthoic acids have mobilities comparable to those of the dimethylbenzoic acids.

TABLE 1.

Acid	Mean Λ_0 (acid)	10^5K therm.	10^5K classical	Earlier values of 10^5K
o-Ethylbenzoic	379·2	16·1	16·3	17 [1]
o-*iso*Propylbenzoic	378·1	$23·1_5$	23·5	—
o-*tert*.-Butylbenzoic	376·0	29·2	29·8	35·1 [4]
2 : 3-Dimethylbenzoic	379·7	18·3	18·7	—
2 : 4-Dimethylbenzoic	379·9	6·57	6·69	9·0 [1]
2 : 5-Dimethylbenzoic	379·9	$10·5_5$	10·8	12·0 [1]
2 : 6-Dimethylbenzoic	379·4	56·8	58·1	62 [3]
3 : 4-Dimethylbenzoic	379·5	3·91	3·97	—
3 : 5-Dimethylbenzoic	379·0	5·00	5·07	4·8,[1] 7·3 [2]
2 : 4 : 6-Trimethylbenzoic	376·9	36·6	37·4	38 [1, 3]
4-*tert*.-Butyl-2 : 6-dimethylbenzoic	376·5	36·1	36·4	—
1-Naphthoic	379·4	20·2	20·3	20·4 [1]
2-Naphthoic	379·2	6·90	6·96	6·78,[1] 5·23 [5]

[1] Bethmann, *Z. physikal. Chem.*, 1890, **5**, 385. [2] Pfaff, Diss., Heidelberg (1897). [3] Breed, Diss., Bryn Mawr (1901). [4] Shoesmith and Mackie, *J.*, 1936, 300. [5] Bader, *Z. physikal. Chem.*, 1890, **6**, 289.

Values of $10^5K_{\text{therm.}}$ for comparison: benzoic acid, 6·27; *o*-, *m*- and *p*-toluic acids, $12·3_6$, 5·35, and 4·24, respectively; 4-*tert*.-butylbenzoic acid, 3·98.

EXPERIMENTAL

Measurement of Conductivity.—The bridge network (based essentially on that of Jones and Josephs, *J. Amer. Chem. Soc.*, 1928, **50**, 1049), oscillator, and amplifier were similar to those described by Dippy and Hughes (*J.*, 1954, 953). A six-decade resistance box (max. resistance 111,111 ohms) was used in series with a single-decade megohm box.

The cells, capped and of symmetrical bottle design, were of Pyrex glass and had capacities of 60—90 ml. (that of the lowest cell-constant having the greatest capacity). The stout greyed-platinum electrodes (Jones and Bollinger, *J. Amer. Chem. Soc.*, 1931, **53**, 411) were mounted rigidly by means of small Pyrex struts at distances of approx. 0·5, 1·0, and 1·5 cm.

TABLE 2.

Acid	M. p. (corr.)	Acid	M. p. (corr.)
o-Ethylbenzoic	65·6°	3 : 4-Dimethylbenzoic	168·0—168·5
o-*iso*Propylbenzoic	59·4—59·9	3 : 5-Dimethylbenzoic	171·2—171·7
o-*tert*.-Butylbenzoic	68·5	2 : 4 : 6-Trimethylbenzoic	156·6—157·1
2 : 3-Dimethylbenzoic	144·5—145·0	4-*tert*.-Butyl-2 : 6-dimethylbenzoic	168·0—169·0
2 : 4-Dimethylbenzoic	125·0—126·0	1-Naphthoic	160·3
2 : 5-Dimethylbenzoic	134·0—134·4	2-Naphthoic	184·2
2 : 6-Dimethylbenzoic	116·3—116·7		

apart in the acid cells and 1·0 cm. apart in the sodium salt cell. The interiors of the cells were first treated with pure acetone and alcohol, and then allowed to stand for several weeks filled with conductivity water which was changed frequently. The cell leads were of amalgamated copper wire dipping into mercury cups immersed in the water-thermostat regulated to 25° (±0·005°).

For the basic cell-constant determination, the specific conductance given by Jones and Prendergast (*ibid.*, 1937, **59**, 731) for a pure 0·01D-potassium chloride solution was employed. The calibration cell had a constant of 0·25926 ± 0·00006 and had a 5-figure numerical resistance when filled with 0·01D-potassium chloride. The other cells were calibrated against this using approximately 0·002N-, 0·001N-, and 0·0002N-potassium chloride solutions, by the method of intermediate cell. The agreement obtained when different cells were used to determine the specific conductance of a given solution (Table 3) confirms the validity of the calibration and, moreover, demonstrates the freedom of greyed electrodes from serious deviations due to adsorption (Jones and Bollinger, *loc. cit.*).

The conductivity water (κ = 0·7—0·9 gemmho) was supplied by an improved form of the still described in earlier work in this series.

Stock solutions of acids of molality ranging from 0·01 to 0·0001 were prepared, either by dilution of stock solutions (cf. earlier papers in this series) or directly from small quantities of

TABLE 3.

Cell const.	10^3C (equiv./l.)	Λ	10^5K class.	10^5K therm.	Cell const.	10^3C (equiv./l.)	Λ	10^5K class.	10^5K therm.
				o-*Ethylbenzoic acid*					
0·03764	0·6883	145·5	16·5	16·1	0·03764	0·1651	233·5	16·3	16·1
	0·5349	160·0	16·5	$16·1_5$		0·1400	243·5	16·1	16·0
	0·3907	178·5	16·4	16·1		0·1010	264·3	16·2	$16·0_5$
	0·1704	231·0	16·2	16·0		0·08304	276·2	16·2	16·1
				o-iso*Propylbenzoic acid*					
0·03759	0·7134	164·2	23·8	$23·2_5$	0·03759	0·2774	222·3	(23·3)	(23·0)
	0·4791	188·0	23·5	23·1		0·2708	224·4	23·5	23·2
	0·3639	205·6	23·6	$23·1_5$		0·2534	227·9	23·2	(22·8)
	0·3349	210·9	23·6	23·2		0·1702	253·8	23·3	23·1
				o-tert.-*Butylbenzoic acid*					
0·03759	1·035	155·4	30·1	29·3	0·03759	0·5301	195·3	29·8	$29·1_5$
	0·8596	165·8	29·9	29·2		0·4203	209·9	29·6	$29·1_5$
	0·7976	170·2	29·9	$29·2_5$		0·3512	221·3	29·5	29·1
	0·7455	174·2	29·8	29·2		0·3209	227·0	29·5	$29·2_5$
	0·5791	189·8	29·8	29·2		0·2903	233·3	29·4	$29·1_5$
				2 : 3-*Dimethylbenzoic acid*					
0·09146	2·167	96·59	18·8	18·2	0·03764	0·3729	190·0	18·7	18·4
	1·512	112·7	19·0	18·4		0·3082	201·9	18·6	$18·3_5$
	1·091	128·2	18·8	$18·3_5$	0·09146 }	0·2644	{ 211·1	18·4	18·2
	0·8608	140·6	18·7	18·3	0·03764 }		{ 210·9	18·3	18·2
	0·6878	153·1	18·7	18·3					
				2 : 4-*Dimethylbenzoic acid*					
0·09146	1·056	84·54	6·73	6·57	0·03764	0·6760	102·3	6·71	$6·58_5$
	0·8845	91·10	6·69	$6·55_5$		0·5463	111·5	(6·66)	(6·53)
	0·8336	93·63	6·72	6·58		0·3676	130·9	6·66	6·56
	0·8000	94·87	(6·65)	(6·51)		0·3220	137·8	6·65	$6·55_5$
				2 : 5-*Dimethylbenzoic acid*					
0·09146	1·443	91·19	10·9	$10·6_5$	0·03764	0·6316	127·2	10·7	$10·4_5$
	1·073	101·1	10·9	$10·6_5$	0·09146 }	0·5749	{ 132·2	10·7	$10·4_5$
	1·034	104·9	10·9	10·6	0·03764 }		{ 132·2	10·7	$10·4_5$
	0·6562	125·8	10·8	$10·5_5$	0·03764	0·4652	144·1	10·8	10·6
	0·6316	127·2	10·7	$10·4_5$		0·2078	191·0	(10·6)	(10·4)
				2 : 6-*Dimethylbenzoic acid*					
0·03764	1·257	185·3	58·6	56·8	0·03764	0·5643	236·0	57·8	$56·7_5$
	1·173	189·5	58·5	56·7		0·5034	243·5	57·9	$56·8_5$
	0·9860	200·2	(58·1)	(56·6)		0·4267	254·0	57·9	$56·7_5$
	0·9699	201·5	58·3	56·8		0·3864	259·7	57·4	56·7
	0·8449	210·4	58·3	$56·8_5$		0·2968	275·3	(57·0)	(56·4)
	0·6024	231·9	57·9	$56·8_5$					
				3 : 4-*Dimethylbenzoic acid*					
0·09146	0·7315	78·80	3·98	3·91	0·03764	0·4546	96·40	(3·93)	(3·87)
	0·7225	79·12	3·97	3·90		0·4883	93·97	3·98	$3·91_5$
	0·6492	82·92	3·96	3·90		0·4524	97·05	3·98	$3·91_5$
	0·6476	83·26	3·99	3·92		0·3689	105·8	3·97	3·91
0·03764	0·6182	84·92	3·99	3·92		0·2360	126·6	3·94	3·89
				3 : 5-*Dimethylbenzoic acid*					
0·03764	0·5644	97·63	5·04	4·96	0·03764	0·3370	121·2	5·08	$4·99_5$
	0·4684	105·9	5·08	5·00		0·3308	122·2	5·08	5·00
	0·4359	108·9	5·05	4·96		0·2589	134·6	5·07	5·00
	0·3951	113·6	5·07	$4·99_5$		0·2185	143·7	5·06	5·00
	0·3882	114·7	5·10	5·02		0·1716	157·4	5·06	5·01
				2 : 4 : 6-*Trimethylbenzoic acid*					
0·03764	1·347	153·5	37·7	36·6	0·03764	0·7779	186·0	37·4	$36·6_5$
	1·103	165·0	37·6	36·6		0·7382	189·2	37·4	36·6
	1·065	167·2	37·7	36·6		0·5491	207·9	37·3	36·6
	0·9304	175·2	37·6	$36·6_5$		0·4515	220·3	37·1	36·6
	0·8036	184·1	37·5	36·6		0·2142	267·1	36·9	36·6

TABLE 3. (*Continued.*)

Cell const.	10^3C (equiv./l.)	Λ	10^5K class.	10^5K therm.	Cell const.	10^3C (equiv./l.)	Λ	10^5K class.	10^5K therm.
				4-tert.-*Butyl*-2 : 6-*dimethylbenzoic acid*					
0·09146	0·9133	174·4	36·3	35·6	0·03764	0·2329	258·8	35·3	35·1
	0·5864	204·1	37·6	36·8	0·09146		259·0	35·3	35·1
	0·5550	206·3	36·9	36·1	0·03764	0·2135	265·3	35·9	35·7
	0·3431	238·7	37·6	37·1$_5$	0·09146		265·4	35·9	35·7
	0·2951	242·8	(34·5)	(34·1)					
				1-*Naphthoic acid*					
0·07322	0·2076	233·5	20·5	20·2	0·07322	0·1336	260·9	20·2	20·1
	0·2038	234·1	20·3	20·1		0·1309	261·6	20·0	20·0
	0·1686	246·6	20·4	20·2		0·1308	261·4	(20·0)	(19·9)
	0·1578	251·0	20·4	20·2		0·1292	263·5	20·4	20·3
	0·1582	250·7	20·4	20·2		0·1060	275·1	20·3	20·3
	0·1338	260·6	20·2	20·0		0·09419	281·2	20·3	20·3
				2-*Naphthoic acid*					
0·07322	0·1857	171·4	(6·92)	(6·84)	0·07322	0·1453	186·7	6·94	6·88
	0·1645	179·1	6·96	6·89		0·1368	190·6	6·95	6·92
	0·1637	179·8	7·00	6·92		0·1184	199·7	6·94	6·89
	0·1534	183·7	7·00	6·92		0·1157	201·4	6·96	6·90

solid acid weighed on a micro-balance [subsequent determination of density (25°) gave the concentration (w./v.)]. The latter method was adopted where enough material was available; capped Pyrex conical flasks used for preparing the solutions had capacities from 250 to 2000 ml., and were initially cleaned with chromic acid and subsequently " seasoned " for 3 months with conductivity water.

The sodium salts were prepared in solution by the addition of a calculated weight of standard aqueous sodium hydroxide (*ca.* 0·01N), made by dissolving washed " AnalaR " sodium hydroxide pellets in water of known low conductance in a 2-litre flask fitted with a siphon and a soda-lime tube, to a known weight of the solid acid. The alkaline solution was standardised with hydrochloric acid (prepared from constant-boiling hydrochloric acid by weight dilution), phenol red being used as indicator. Capped 1-litre flasks were employed in the making of these salt solutions, and the amount of alkali employed was approximately 0·2% less than that required for equivalence (solution density of alkali relates to room temperature). It was thus ensured that the solution remained slightly acidic throughout the dilution range; the presence of a minute excess of the weak acid (unlike a trace of alkali) has no appreciable effect on the conductance of the solution. The salt solution was then diluted (by weight) to about 0·0025 g.-equiv./l., and the precise concentration calculated from the weight of sodium hydroxide added. The subsequent procedure was that described in earlier papers for the determination of $\Lambda_{0(\text{acid})}$.

The cells were filled by the method recommended by Ives and Riley (*J.*, 1931, 1998). No water correction was applied to acid conductance measurements. All weighings were corrected to *vacuo*.

Preparation and Purification of Materials.—*o*-Ethylbenzoic acid was obtained in 60% yield from *o*-bromoethylbenzene by a Grignard synthesis. Ethylbenzene was nitrated (Cline and Emmet, *J. Amer. Chem. Soc.*, 1927, **49**, 3150), and fractionation of the product yielded *o*-nitroethylbenzene (50%), b. p. 132—134°/36—37 mm. Reduction of this with iron and hydrochloric acid gave *o*-ethylaniline quantitatively which was converted by a Gattermann reaction into *o*-bromoethylbenzene, b. p. 88—89°/15 mm.

*o-iso*Propyl-, *o-tert.*-butyl-, 2 : 6-dimethyl-, and 2 : 4 : 6-trimethyl-benzoic acids were kindly supplied by Prof. M. Crawford and Dr. F. H. C. Stewart, whom we thank.

2 : 3-Dimethyl-, 2 : 4-dimethyl-, 2 : 5-dimethyl-, 3 : 4-dimethyl-, and 3 : 5-dimethyl-benzoic acids were provided by Professor H. A. Smith and Dr. J. A. Stansfield to whom grateful acknowledgment is made.

4-*tert.*-Butyl-2 : 6-dimethylbenzoic acid was obtained from 1-bromo-4-*tert.*-butyl-2 : 6-dimethylbenzene (Nightingale and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 101) by a Grignard synthesis (Crawford and Stewart, *J.*, 1952, 4443). The naphthoic acids were purchased.

All the acids were repeatedly recrystallised from conductivity water and finally stored for at least two weeks in desiccators. All specimens were well authenticated by both m. p. and

determination of the equivalent. The m. p.s recorded in Table 2 were those of the final specimens, before measurement; they are in close agreement with the best values in the literature (Crawford and Stewart, *loc. cit.*, and Smith and Stansfield, *J. Amer. Chem. Soc.*, 1949, **71**, 81, for the alkylbenzoic acids, and Bethmann, *loc. cit.*, for the naphthoic acids).

Discussion

The literature shows that the substituents so far examined enhance the strength of benzoic acid (in water) inordinately when introduced into the *ortho*-position, and a similar observation is made when such substituents occupy the β-position in ethylenic acids of *cis*-configuration. The principal factors responsible for this have been discussed by Ingold ("Structure and Mechanism in Organic Chemistry," B. Bell and Son Ltd., London, 1953). That diverse steric factors operate in *o*-substituted benzoic acids becomes manifest by examination of their behaviour in solvents of widely differing ionising capacities (*i.e.* varying in dielectric constant and in solvating character). The linear plot of log K/K_u against $1/D$ (K/K_u being the ratio of acid strength to that of the parent acid) gives a positive slope with *m*- and *p*-methoxy-, -chloro-, -bromo-, -iodo-, and -nitro-benzoic acids, and a negative slope with the *o*-isomers, whereas the converse holds for hydroxybenzoic acids (Elliott and Kilpatrick *J. Phys. Chem.*, 1941, **45**, 3). This is noteworthy in view of the general belief that the abnormally high dissociation constant of salicylic acid is due to the specific hydrogen bonding between the two substituents in the anion in that instance, whereas the abnormality of the other *o*-substituted benzoic acids mentioned above has been attributed to steric inhibition of mesomerism (Ingold, *loc. cit.*; cf. Baddeley, *Nature*, 1939, **144**, 444), an influence expected by Birtles and Hampson (*J.*, 1937, 10) and first demonstrated by them in a study of the dipole moments of substituted durenes. It should also be noted that to account for the relatively high K_1 value and relatively low K_2 value for maleic acid compared with fumaric acid both kinds of group interaction have been invoked, *i.e.* hydrogen bonding (Hunter, *Chem. and Ind.*, 1953, 155) and steric inhibition of mesomerism (Crawford, *ibid.*, p. 797) (see also, the first and second dissociation constants of phthalic acid.

It is less certain whether there is a special hydrogen bonding between methyl and carboxyl groups (despite hyperconjugation) although this suggestion was advanced by Dippy *et al.* (*J.*, 1937, 1421) to account for the abnormal dissociation constant of *o*-toluic acid in water. Such a tendency might well be contributory but it is now considered not to be dominant. The strengths of the benzoic acids substituted at the *o*-position by methyl, ethyl, *iso*propyl, and *tert.*-butyl progressively increase (see Table 1), and the fact that the abnormality is most marked with *tert.*-butyl seems to render the original hydrogen bond suggestion unacceptable as a principal factor here. Moreover, *o*-phenyl and *o*-phenoxyl groups have a comparable effect upon the strength of benzoic acid, referred to as unity in the following table of K/K_u values:

	Me *	Et	Pr^i	Bu^t	PhO *	Ph *
o-	1·97	2·57	3·69	4·65	4·74	5·53
p-	0·676	0·707	0·707	0·635	0·478	—

* Dippy, *Chem. Reviews*, 1939, **25**, 181.

It is satisfactory also to note that whereas the strengths of 2-naphthoic and benzoic acids are closely alike, that for 1-naphthoic acid lies between the values for *o*-ethyl- and *o*-*iso*-propyl-benzoic acids (see Table 1).

These observations are consistent with the theory of steric inhibition of mesomerism. The conjugation existing between carboxyl and the benzene ring, to be fully functional, demands the favoured position provided by co-planarity. If obstruction is exerted by a sufficiently bulky group in the *ortho*-position there will be a twisting of the carboxyl group out of the plane of the ring, so that the effective conjugation of carboxyl with the aromatic nucleus becomes weaker. In other words, the $-M$ effect of carboxyl, responsible for the relative weakness of benzoic acid (Dippy, *loc. cit.*), is hampered in its operation; consequently, the greater the obstruction, as with increasing size of alkyl group, the stronger the acid.

The strengths of the benzoic acids containing two *o*-methyl substituents (see Table 1) may be interpreted along similar lines. The conjugation of carboxyl and aromatic nucleus is stronger in *p*-toluic acid and *p-tert.*-butylbenzoic acid than in benzoic acid. In short, there will be a greater multiplicity (electron content) of the bond between carboxyl-carbon and aryl-carbon in the *p*-alkyl-substituted acids. Thus the twisting, even if occurring to the same extent, will creat different constraints in the three different systems, and consequently it is necessary to trace the inhibition by relating the increase in dissociation constant to the appropriate parent acid in each case. Such an analysis reveals a striking reproduction of the effect as the following table of K/K_u values shows (where the K of each parent acid is referred to as unity).

Substituents	Benzoic	*p*-Toluic	*p-tert.*-Butylbenzoic acid
2-Methyl	1·97	1·55	—
2 : 6-Dimethyl	9·06	8·63	9·20

There is in effect a case for less easy twisting of carboxyl out of the plane of the ring in *p*-toluic acid (relative to benzoic acid), and it is noteworthy that the introduction of methyl to an *ortho*-position here increases K by a factor of about 1·6, whereas similar substitution in benzoic acid increases K by a factor of 2. Similarly, a second *o*-methyl group is responsible for an overall increase by a factor 8·6 in the former system and by 9·1 in the latter.

A further analysis is to trace the influence of the substitution of methyl and of *tert.*-butyl groups in the 4-positions of benzoic acid and 2 : 6-dimethylbenzoic acid, respectively. A remarkable similarity in the increments in free energy of ionisation is noted from the following table. Introduction of methyl into the 4-position of *o*-toluic acid has a qualitatively similar, if greater, effect. The current theory offers no satisfactory explanation of this regularity, although we consider that the feature is more than fortuitous.

Parent acid	4-Substituent	$\Delta G°$ subst. $-$ $\Delta G°$ parent (cals. mole^{-1})
Benzoic	Methyl	232
Benzoic	*tert.*-Butyl	269
2 : 6-Dimethylbenzoic	Methyl	260
2 : 6-Dimethylbenzoic	*tert.*-Butyl	269

The absence of considerations of steric orientation in phenol (Baddeley, *loc. cit.*) makes the values of the acid strengths of methyl substituted phenols, published by Sprengling and Lewis (*J. Amer. Chem. Soc.*, 1953, **75**, 5709), particularly interesting. The steady diminution of strength shown below (H representing parent phenol) makes an impressive contrast to the benzoic acid series. Doubtless the controlling factors here are simply the formal $+I$, $+M$ effects of the methyl group.

	H	*p*-Methyl	*o*-Methyl	2 : 4-Dimethyl	2 : 4 : 6-Trimethyl
pK	9·85	10·10	10·19	10·49	10·80

An interesting result is that for 2 : 3-dimethylbenzoic acid; the enhancement factor here is approximately 3 as distinct from the factor of <2 shown by 2 : 5-dimethylbenzoic acid (related to benzoic acid as parent). This might be connected with the fact that in the 2 : 3-disubstituted acid there are two steric interactions between the three vicinal groups. The repulsion between the adjacent electropositive methyl groups would cause the 2-methyl group to obstruct carboxyl more than in the usual model, and the measured strength shows it to be about as effective as 2-ethyl. An interesting observation having a bearing on this feature can be made by examination of the acid strengths listed by Shorter and Stubbs (*J.*, 1949, 1180); although these data are inaccurate, they serve to reveal that isomeric 2 : 3- and 2 : 5-disubstituted benzoic acids almost always have widely different strengths.

Observations by Crawford and Stewart (*J.*, 1953, 288) on the solubilities of the copper salts of some of the acids discussed here may be correlated with this work. These authors ascribe the unusually high solubilities in benzene–ethanol of copper salts of *o*-methylbenzoic acids to steric inhibition of mesomerism which is responsible for a weakening of the crystal structure.

There remain the 3 : 4- and 3 : 5-dimethylbenzoic acids whose strengths are less than that of benzoic acid, and fall below that for *m*-toluic acid by amounts expected from the operation of formal electron disturbances. It is relevant to point out here, however, that in the di- and tri-substituted benzoic acids, the only system in which steric interaction of groups cannot intervene is the 3 : 5-disubstituted benzoic acid. It is for this reason that the additivity principle for benzoic acids containing more than one substituent, explored by Shorter and Stubbs (*loc. cit.*), appeared to apply well to the 3 : 5-disubstituted acids. In a 3 : 4-disubstituted benzoic acid the group in the 3-position might inhibit the operation of the *M* effect of the group in the 4-position and this would be reflected in *K*; with some substituents (other than methyl) this effect could be pronounced.

The changes in the characteristics observed by Moser and Kohlenburgh (*J.*, 1951, 805) in the ultra-violet absorption spectra of certain methylbenzoic acids are relevant. They ascribe the changes in intensity of the so-called *B* band ($\lambda_{max.}$ 2280—2320 Å) to steric interference with resonance. It was shown that absorption in this region was strong in the cases of benzoic acid and *m*- and *p*-toluic acids (being most marked in the last), whilst the intensity fell with *o*-toluic acid, and the characteristic disappeared in 2 : 6-dimethylbenzoic acid. We have confirmed these findings, and have examined (over the appropriate, if narrow, range) the ultra-violet absorption spectra of some of the other acids whose strengths are recorded here. We find that 2 : 4 : 6-trimethylbenzoic acid compares with 2 : 6-dimethylbenzoic acid, but that 2 : 4-dimethylbenzoic acid is like *o*-toluic acid in showing a noticeable *B* band. 2 : 3-Dimethylbenzoic acid occupies an intermediate position in that here the *B* band appears only as a weak inflexion. There is thus an apparent correspondence between the conclusions arising from these spectral measurements and those derived from acid dissociation constant data.

CHEMISTRY DEPARTMENT, CHELSEA POLYTECHNIC,
LONDON, S.W.3.

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Preparation and Reactions of Diphenylene.

By WILSON BAKER, (MISS) M. P. V. BOARLAND, and J. F. W. MCOMIE.

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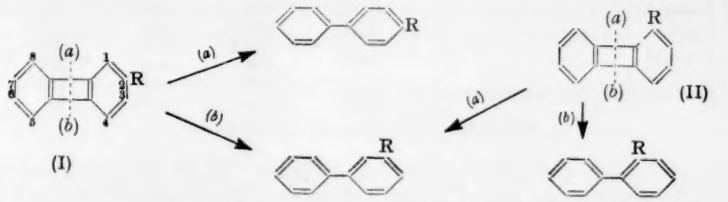
The synthesis of diphenylene (I; R = H) has been improved. With acetyl chloride and aluminium chloride it gives 2-acetyldiphenylene, in agreement with predictions based on wave-mechanics. The acetyl derivative has been converted *via* its oxime and the 2-acetamido-compound, into 2-aminodiphenylene, and into diphenylene-2-carboxylic acid by reaction with sodium hypochlorite. Reduction of 2-acetyldiphenylene by Raney nickel containing adsorbed hydrogen gives a mixture of 3- and 4-acetyldiphenyl, thus establishing the position of the acetyl group.

DIPHENYLENE (I; R = H) was first prepared by Lothrop (*J. Amer. Chem. Soc.*, 1941, **63**, 1187) by distillation of 2 : 2′-dibromo- or better 2 : 2′-di-iodo-diphenyl with cuprous oxide, the yield from the di-iododiphenyl being 15%. It was later obtained from 2 : 2′-dibromodiphenyl in 4% yield by reaction with magnesium and anhydrous cupric chloride (Rapson, Shuttleworth, and van Niekerk, *J.*, 1943, 326). The early history of this hydrocarbon has been given by Lothrop (*loc. cit.*) and by Baker (*J.*, 1945, 258), and the latter has discussed the evidence confirming the structure (I; R = H). Lothrop (*loc. cit.*; *J. Amer. Chem. Soc.*, 1942, **64**, 1698) has prepared 1 : 8- and 2 : 7-dimethyldiphenylene and 2 : 7-dimethoxydiphenylene by the synthesis used for the parent compound.

Diphenylene is representative of the only known type of compound in which there is a four-membered ring fused to a benzene nucleus, and it may also be regarded as a derivative of the unknown *cyclo*butadiene, as shown in formula (I), which represents one of the five purely covalent canonical forms of the molecule. With the exception of preliminary experiments on its catalytic reduction, the chemical properties of diphenylene have not been previously investigated, and the present work was undertaken primarily with the

object of studying substitution in the diphenylene nucleus. A further objective was the degradation of one of the benzene nuclei of diphenylene to give a derivative of benzo*cyclo*butene or of benzo*cyclo*butadiene.

The preparation of diphenylene from *o*-chloronitrobenzene *via* 2 : 2′-dinitrodiphenyl, 2 : 2′-diaminodiphenyl, and diphenyl-2 : 2′-iodonium iodide has been improved at each



stage, and special attention has been paid to the final distillation of the iodonium iodide (which first passes into 2 : 2′-di-iododiphenyl) with cuprous oxide, whereby in this last stage the rather variable yield has been raised to an average of 21%. The overall yield of diphenylene from *o*-chloronitrobenzene is now 6—9% (Lothrop, *ca.* 2%). We have been unable to prepare diphenylene (*a*) by heating *o*-di-iodobenzene with cuprous oxide, (*b*) by heating 2-*N*-nitrosoacetamidodiphenyl, (*c*) by electrolysis of aqueous sodium 2 : 2′-diphenate (cf. Weedon, *Quart. Reviews*, 1952, **6**, 380), or (*d*) by heating 2 : 2′-diphenic acid with cuprous oxide or copper chromite; the last reaction gave diphenyl, fluorenone, and the lactone of 2-carboxy-2′-hydroxydiphenyl.

Lothrop found that catalytic reduction of diphenylene over hot copper gave 30% of diphenyl, but an 85% yield is obtained in alcoholic solution in presence of Raney nickel (Baker, *loc. cit.*, p. 266; see Experimental). In presence of a palladium–charcoal catalyst, the reduction proceeds further (*ca.* 3 mols. of hydrogen are absorbed) owing to reduction of the diphenyl to phenyl*cyclo*-hexane and -hexenes. When diphenylene is reduced with sodium and liquid ammonia, a 30% yield of diphenyl is obtained, but reduction products of diphenyl are also obtained in quantity (for reduction of diphenyl with this reagent see Hückel and Bretschneider, *Annalen*, 1939, **540**, 157). Diphenylene is not reduced by amalgamated zinc and hydrochloric acid, or by *cyclo*hexadiene in presence of palladium (cf. Linstead, *Nature*, 1952, **169**, 100).

Diphenylene reacts with acetyl chloride (a large excess is required) and aluminium chloride in carbon disulphide to give 2-acetyldiphenylene (I; R = Ac; for proof of orientation see below) in 58% yield, and a diacetyldiphenylene, probably 2 : 6-diacetyldiphenylene, in 14% yield. The oxime of 2-acetyldiphenylene undergoes the Beckmann rearrangement, best with polyphosphoric acid (Horning and Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680), and the resulting 2-acetamidodiphenylene is hydrolysed to 2-aminodiphenylene (I; R = NH_2). Oxidation of 2-acetyldiphenylene with sodium hypochlorite gives diphenylene-2-carboxylic acid (I; R = CO_2H), which has been converted into the methyl ester with diazomethane.

The orientation of the acetyldiphenylene depends on reductive cleavage of the 4-membered ring to give a derivative of diphenyl. A 1-substituted diphenylene (II) could give a 2- and a 3-substituted diphenyl as shown. A 2-substituted diphenylene (I) could similarly give a 3- and a 4-substituted diphenyl. Hence only the isolation of a 2- or a 4-substituted diphenyl could give conclusive evidence of orientation. Acetamidodiphenylene resisted hydrogenation in presence of nickel, palladium, or platinum catalysts. When diphenylenecarboxylic acid was warmed with sodium amalgam in aqueous dioxan, or with Raney nickel in ethanol, the yellow colour typical of the diphenylene system was discharged, but no diphenylcarboxylic acid could be isolated, and an examination of the ultra-violet absorption spectrum of the product in conjunction with the spectra of the three authentic diphenylcarboxylic acids (see Table 1) gave no conclusive information. When, however, acetyldiphenylene was warmed with Raney nickel in ethanol, a mixture of acetyldiphenyls was formed. Both chromatographic methods and ultra-violet absorption spectra (see Table 1) of the derived 2 : 4-dinitrophenylhydrazones showed conclusively

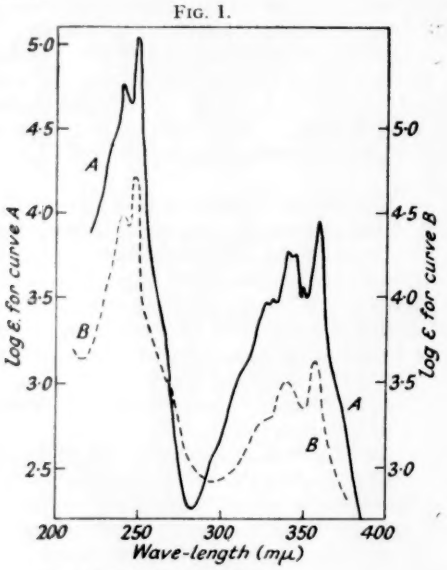
TABLE 1. *Ultra-violet absorption characteristics of diphenyl derivatives.*

Substituents *	Solvent	$\lambda_{max.}$ (mμ)	$\log_{10} \varepsilon_{max.}$	$\lambda_{min.}$ (mμ)	$\log_{10} \varepsilon_{min.}$
4-Acetyl	EtOH	282·5	4·39	239	3·40
2-Carboxylic acid	EtOH	245	4·07	235	4·07
3-Carboxylic acid	EtOH	250	4·22	241	4·21
4-Carboxylic acid	EtOH	264·5	4·42	228	3·73
D.N.P. of 2-acetyl	C_6H_6	369	4·34	310	3·55
D.N.P. of 3-acetyl	C_6H_6	376·5	4·37	316	3·55
D.N.P. of 4-acetyl	C_6H_6	299·5	4·12	282	4·06
		384	4·40	327	3·73
D.N.P. of product from acetyldiphenylene ...	C_6H_6	296	4·03	324	3·72
		381	4·39	—	—

* D.N.P. = 2 : 4-dinitrophenylhydrazone.

the presence of the 3- and the 4-substituted diphenyl. From this it follows that in the Friedel–Crafts reaction the acetyl group had entered the 2-position of the diphenylene nucleus.

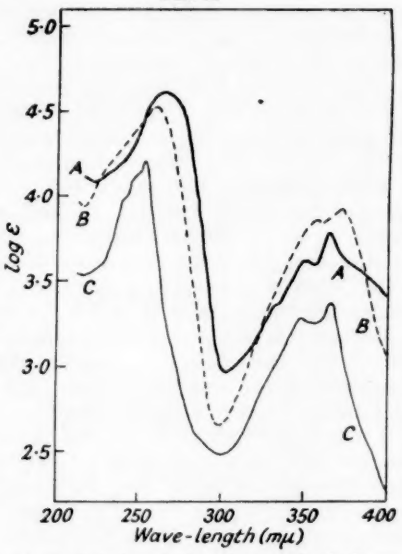
FIG. 1.



A, Diphenylene in ethanol.
B, 2-Aminodiphenylene in N-HCl.

Note. *The log ε scales for A and B are shown on the left- and right-hand sides respectively of the Figure.*

FIG. 2.



A, B, C, 2-Acetyl-, 2-amino-, and x*-hydroxydiphenylene respectively.*

This orientation of the acetyldiphenylene (I; R = Ac) is in agreement with Brown's theoretical predictions (*Trans. Faraday Soc.*, 1949, **45**, 296; 1950, **46**, 146; see also Waser and Schomaker, *J. Amer. Chem. Soc.*, 1943, **65**, 1451) based on wave-mechanical calculations. The result cannot, however, be claimed as confirming the predictions, because Friedel–Crafts acylation may occur at different positions according to the reaction conditions (*e.g.*, in the case of naphthalene; see Thomas, "Anhydrous Aluminium Chloride in Organic Chemistry," Reinhold Publ. Corp., New York, 1941, pp. 271 *et seq.*).

Apart from nuclear acetylation, no other simple monosubstitution into the nucleus of diphenylene has been achieved. Bromination and nitration gave inseparable mixtures; sulphonation gave a disulphonic acid of unknown orientation. Ozonisation in carbon tetrachloride yielded a complex mixture of carbonyl compounds. With lead tetra-acetate in acetic acid diphenylene gave a 1·5% yield of a product which appears, from its ultra-violet absorption spectrum, to be a hydroxydiphenylene (see Fig. 2), and the similarity

of the spectrum to that of 2-aminodiphenylene suggests further that the hydroxyl group is in position 2. 2-Acetyldiphenylene was not converted into 2-acetoxydiphenylene by hydrogen peroxide in acetic acid (cf. Ballio, *Gazzetta*, 1949, **79**, 924).

From the catalytic reduction of 2 : 2′-dinitrodiphenyl in presence of Raney nickel in ethanol–acetic acid at 30 atmospheres was isolated a crystalline complex of 2 mols. of 2 : 2′-diaminodiphenyl with 1 mol. of nickel acetate. This substance was also obtained under similar conditions from 2 : 2′-diaminodiphenyl and nickel acetate, the identity of the two specimens being established by *X*-ray powder photographs kindly taken by Dr. T. H. Bevan.

The ultra-violet absorption spectrum of diphenylene in hexane solution has been discussed by Carr, Pickett, and Voris (*J. Amer. Chem. Soc.*, 1941, **63**, 3231). The spectrum in ethanol is shown in Fig. 1 (see also Table 2); it agrees well with that obtained in hexane except for a slight shift in wave-length due to the change in solvent. The split peak in the region 330—400 mμ appears to be characteristic of simple diphenylene derivatives; it occurs in all the derivatives so far examined, except the 2 : 4-dinitrophenylhydrazone of 2-acetyldiphenylene where it is probably masked by the absorption of the dinitrophenylhydrazine residue (cf. Roberts and Green, *ibid.*, 1946, **68**, 214). The spectrum of 2-aminodiphenylene in hydrochloric acid (Fig. 1) closely resembles that of the parent hydrocarbon, but the spectrum of the free base in ethanol (Fig. 2) is much less complex; similar behaviour has been observed with other aromatic amines, *e.g.*, 4-aminopyrene (Jones, *ibid.*, 1945, **67**, 2127). The spectra of the oxime of 2-acetyldiphenylene, of 2-acetamido-, 2-carboxy-, and 2-methoxycarbonyl-diphenylene are very similar to that of the 2-acetyl compound (Fig. 2) and are not illustrated graphically.

TABLE 2. *Ultra-violet absorption characteristics of diphenylene derivatives.*

Substituents *	Solvent	λ(mμ)	$\log_{10}\varepsilon_{max.}$	λ(mμ)	$\log_{10}\varepsilon_{max.}$
None	EtOH	239	4·77	339	3·79
		248	5·05	343	3·76
		326	3·47	348	3·58
		330	3·49	358	3·97
2-Acetyl	EtOH	236	4·61	348	3·63
				363	3·80
Oxime of 2-acetyl	EtOH	237·5	4·40	355	4·86
		263	4·67	370	3·90
2-Acetamido	EtOH	237	4·36	349·5	3·97
		259	4·81	368	4·07
2-Amino	EtOH	258·5	4·53	357	3·85
				371	3·93
2-Amino	N-HCl	239·5	4·49	330·5	3·30
		248	4·73	339	3·53
				357	3·65
2-Carboxy	EtOH	256·5	4·87	347	3·75
				362	3·91
2-Methoxycarbonyl	EtOH	260	4·77	346	3·66
				360·5	3·83
D.N.P. of 2-acetyl	C_6H_6	295	4·20	375	4·31
				415	4·35
x-Hydroxy (?)	EtOH	253	4·70	346·5	3·78
				364	3·87

* D.N.P. = 2 : 4-dinitrophenylhydrazone.

EXPERIMENTAL

The temperatures recorded for sublimations are those of the heating baths.

Diphenylene.—The modifications of recorded methods are given in the following notes. (1) *2 : 2′-Dinitrodiphenyl.* (*a*) See *Org. Synth.*, 1940, **20**, 45; the weight of copper bronze was reduced to 150 g. per 200 g. of *o*-chloronitrobenzene. The product (58% yield) was recrystallised twice before reduction. (*b*) See von Niementowsky, *Ber.*, 1901, **34**, 3325; copper bronze activated by iodine (Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4219) may replace the freshly precipitated copper powder. Pure 2 : 2′-dinitrodiphenyl is isolated directly in 44—53% yield. (2) *2 : 2′-Diaminodiphenyl.* Catalytic reduction is more convenient than the use of tin and hydrochloric acid. Pure 2 : 2′-dinitrodiphenyl (60 g.) with Raney nickel (15 g.; Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353) suspended in ethanol (400 c.c.) and glacial acetic acid

(10 c.c.) in a steel bomb, was hydrogenated at 110°/30 atm. for 30—40 min. The considerable heat of reaction makes it desirable to interrupt the external heating for 1 hr., after which it is resumed for 4½ hr. The filtered solution was poured into water (2 l.) at 60° with vigorous stirring, and after cooling to 0° gave light brown, or colourless, crystals (36 g., 80%). (3) Diphenyl-2 : 2′-iodonium iodide was prepared from the diamine in 69% yield by Lothrop's method. (4) *Diphenylene.* Pyrolysis of the preceding compound was conducted in a short-necked, 150-c.c. flask fitted with an air-condenser having a pear-shaped bulb close to the ground joint attaching it to the flask. The apparatus was inclined at *ca.* 25° to the horizontal and rotated (*ca.* 100 rev./min.) by a motor attached co-axially to the top of the condenser. The flask dipped into a fusible metal-bath fitted with a lid, and the metal surface was covered with a thick layer of charcoal. The iodonium iodide (10 g.) was powdered with cuprous oxide (80 g.), the mixture heated for a few minutes at 100°/1 mm. in the reaction flask, which was then attached to the condenser and rotated in the metal-bath (pre-heated to 350—360°) for 4 min. The sublimed diphenylene was extracted into methanol (50 c.c.) and steam-distilled, giving diphenylene (1·055 g., 28%), m. p. 95—102°. Two recrystallisations from methanol raised the m. p. to 110—111°.

In a series of 12 runs, the yield of once recrystallised diphenylene, m. p. 106—109°, varied from 15 to 30% (average 21%). The mother-liquors yielded also diphenyl, 2-iododiphenyl, and carbazole. The dark yellow-green residue from the steam-distillation was collected and dissolved in methanol (50 c.c.) (charcoal), and the solution was filtered and concentrated (to *ca.* 20 c.c.), giving 2 : 2′-di-iododiphenyl (*ca.* 1·0 g. from a 10-g. run), m. p. 110°. Phenazone was also isolated as its picrate (cf. Lothrop, *loc. cit.*). The cuprous oxide may be used for at least five experiments without significant loss of activity. The *complex* of diphenylene with 2 : 4 : 7-trinitrofluorenone formed deep scarlet needles (from ethanol), m. p. 154° (decomp.) (Found : C, 64·1; H, 2·9; N, 9·2. $C_{12}H_8,C_{13}H_5O_7N_3$ requires C, 64·25; H, 2·8; N, 9·0%).

Complex of 2 : 2′-*Diaminodiphenyl with Nickel Acetate.*—In some of the reductions of 2 : 2′-dinitrodiphenyl the spent catalyst contained greenish-blue crystals. These were separated by shaking the mixture with chloroform : only the crystals floated. After several repetitions the compound was obtained in a fairly pure state. It was insoluble in the usual organic solvents, could not be recrystallised, and decomposed when boiled with water for 5 min., giving 2 : 2′-diaminodiphenyl (m. p. and mixed m. p. 78—80°) and a solution giving a strong positive reaction with dimethylglyoxime for nickel; the presence of acetate was revealed by the indigo test (Feigl, " Qualitative Analysis by Spot Tests," Elsevier Publ. Co., New York, 1948). These and the analytical results suggested that the blue compound was a 2 : 1 *complex* of 2 : 2′-diaminodiphenyl with nickel acetate (Found, in material in which microscopical examination revealed the presence of traces of nickel : C, 60·8, 60·9; H, 5·4, 5·6; N, 10·9; Ni, 12·2. $C_{28}H_{30}O_4N_4Ni$ requires C, 61·7; H, 5·5; N, 10·3; Ni, 10·8%). The same complex was produced on heating ethanol–acetic acid solutions of nickel acetate and the diamine under pressure as in the catalytic reduction.

Catalytic Reduction of Diphenylene.—Ethanol (35 c.c.) and Raney nickel (0·25 g.) were saturated at room temperature and pressure with hydrogen. Diphenylene (0·5 g.) was then added from a side-arm and the hydrogenation continued (4 hr.) until one equivalent of hydrogen had been absorbed. The solution yielded crude diphenyl (0·43 g.; m. p. 56°), which, after two recrystallisations from aqueous methanol, had m. p. and mixed m. p. 70°.

Reduction by Sodium in Liquid Ammonia.—Liquid ammonia (*ca.* 100 c.c.) was added to a solution of diphenylene (0·30 g.) in ether (25 c.c.), followed by sodium (0·27 g.; 6 equivs.) in small portions. The solution changed in colour through yellow, purple, and deep blue to deep olive-green. Next day the residual solid was treated with water and extracted with ether. Removal of the ether and fractional sublimation yielded diphenyl (0·10 g., 30%), m. p. 66—67° (mixed m. p. with pure diphenyl, 69—70°). The lower- and higher-boiling fractions were unsaturated oils.

2-*Acetyl- and* 2 : 6(?)-*Diacetyl-diphenylene.*—Diphenylene (0·300 g.) was added to finely powdered aluminium chloride (0·300 g., 1·1 equivs.) and acetyl chloride (2·25 g., 10 equivs.) in pure, dry carbon disulphide (40 c.c.), and the mixture, which became deep red, was gently warmed on a water-bath for 1 hr. Next day dilute hydrochloric acid was added and, when the red crystalline aluminium chloride complex had decomposed, the mixture was filtered from the diacetyl derivative (0·066 g.). The filtrate was extracted with carbon disulphide and yielded a solid which was fractionally sublimed, giving diphenylene (collected at 100°/20 mm.) and 2-*acetyldiphenylene* (0·220 g.), m. p. 133—134° (collected at 130°/20 mm.). Recrystallisation from aqueous ethanol gave the pure compound as glistening yellow plates, m. p. 134—135°

(Found: C, 86·4; H, 5·1. $C_{14}H_{10}O$ requires C, 86·6; H, 5·2%). The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid as bright red crystals, m. p. 257—258° (Found: C, 64·3; H, 3·7; N, 14·9. $C_{20}H_{14}O_4N_4$ requires C, 64·2; H, 3·75; N, 14·95%).

The 2 : 6(?)-*diacetyldiphenylene* mentioned above was recrystallised from ethanol and formed deep yellow needles, m. p. 247—248° (Found: C, 81·2; H, 5·0. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%).

2-Acetyldiphenylene gave an *oxime* as fine, pale yellow needles (from aqueous ethanol), m. p. 176° (Found: C, 80·2; H, 5·25; N, 6·8. $C_{14}H_{11}ON$ requires C, 80·4; H, 5·3; N, 6·7%).

2-*Acetamidodiphenylene.*—(a) *By use of polyphosphoric acid* (Horning and Stromberg, *loc. cit.*). The oxime (0·100 g.) was added to polyphosphoric acid (3·0 g.; *ca.* 84% P_4O_{10}), and the mixture kept at 100° for 10 min. The green, viscous solution was diluted and the solid extracted into ether–ethyl acetate (1 : 1), and sublimed. The 2-*acetamidodiphenylene* (0·060 g.; 60%) formed pale yellow plates, which after recrystallisation from aqueous ethanol had m. p. 146—147° (Found: C, 80·4; H, 5·1; N, 6·6. $C_{14}H_{11}ON$ requires C, 80·4; H, 5·3; N, 6·7%).

(b) *By use of phosphorus pentachloride.* Phosphorus pentachloride (0·100 g.) was added to the oxime (0·100 g.) in dry ether and, after 10 minutes' treatment with ice, extraction with ether–ethyl acetate and sublimation gave 2-acetamidodiphenylene (0·040 g.), m. p. 135—138°.

2-*Aminodiphenylene.*—2-Acetamidodiphenylene (0·05 g.) was heated with water (5 c.c.), concentrated hydrochloric acid (5 c.c.), and ethanol (1·0 c.c.) for 1 hr. On cooling, a hydrochloride separated. Addition of excess of dilute sodium hydroxide solution and extraction with ether gave 2-*aminodiphenylene*, which, after two sublimations, formed bright yellow needles (0·03 g.), m. p. 123—124° (Found: C, 86·2; H, 5·5; N, 8·6. $C_{12}H_9N$ requires C, 86·3; H, 5·4; N, 8·4%).

Diphenylene-2-carboxylic Acid.—Chlorine (0·7 g.) was passed into a cooled solution of sodium hydroxide (1·0 g.) in water (10 c.c.); of the resultant solution a portion (4 c.c.) was added to 2-acetyldiphenylene (0·100 g.) in dioxan (6 c.c.) at 70° and the mixture (2 layers) heated on a water-bath for ½ hr. Water was then added to give a homogeneous solution, followed by more sodium hypochlorite solution (2 c.c.), and the heating was continued for ¾ hr. The solution was concentrated under reduced pressure to remove the dioxan, and acidified with concentrated hydrochloric acid, giving a solid (0·090 mg.), m. p. 210—220°. Sublimation at 210°/20 mm., followed by recrystallisation from aqueous methanol, gave *diphenylene-2-carboxylic acid* as yellow prisms, m. p. 223—224° (Found: C, 79·5; H, 4·1. $C_{13}H_8O_2$ requires C, 79·6; H, 4·1%).

The *methyl ester*, prepared by diazomethane, sublimed at 130°/20 mm. as pale yellow plates (0·049 g.), m. p. 106—110°. Recrystallisation from aqueous methanol and a further sublimation raised the m. p. to 114—115° (Found: C, 79·7; H, 4·5. $C_{14}H_{10}O_2$ requires C, 80·1; H, 4·8%).

Orientation of the Acetyldiphenylene.—(1) *Action of Raney nickel on diphenylene.* Raney nickel (Brown, *loc. cit.*) (*ca.* 0·2 g.) was added gradually with shaking to a solution of the ketone (0·100 g.) in ethanol (10 c.c.) at 60° until the yellow colour was discharged. The filtered solution and washings were concentrated, excess of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid was added, and the mixture was boiled for several minutes. The dinitrophenylhydrazones were extracted into benzene, and the dried, concentrated extract passed through a column of alumina, which was eluted with benzene–ether (1 : 1), leaving some strongly adsorbed impurities at the top of the column. The eluate was evaporated and the residue crystallised from acetic acid, giving an orange-red product (0·070 g.), m. p. 170—210°.

(2) *Chromatography.* Chromatography of the 2 : 4-dinitrophenylhydrazones of 2-, 3-, and 4-acetyldiphenyl and of the preceding mixture was carried out on strips of Whatman No. 1 filter paper, the spots being detected by their colour in day-light and in ultra-violet light. On use of light petroleum (b. p. 80—100°) and ether (95 : 5), the R_F values of the 2-, 3-, and 4-isomers were 0·79, 0·45, and 0·35 respectively. The mixture gave spots of R_F value 0·45 and 0·35. The colour of the mixture (orange-red) also indicated that the product had this composition since the 2-, 3-, and 4-isomers are yellow, orange, and red respectively.

(3) *Reference compounds.* Samples of the 2 : 4-dinitrophenylhydrazones of 2-acetyldiphenyl (m. p. 169—170°) and 3-acetyldiphenyl (m. p. 191—192°) were kindly provided by Professor E. Campaigne of Indiana University. The 2 : 4-*dinitrophenylhydrazone* of 4-acetyldiphenyl (for preparation of 4-acetyldiphenyl see Gull and Turner, *J.*, 1929, 491) formed bright red plates, m. p. 238—239°, from acetic acid (Found: C, 64·1; H, 4·0; N, 15·0. $C_{20}H_{16}O_4N_4$ requires C, 63·9; H, 4·3; N, 14·9%).

Sulphonation of Diphenylene.—Diphenylene (0·200 g.) was dissolved in concentrated sulphuric acid (1·0 c.c.) and after 24 hr. the solution was poured into water (20 c.c.) and neutralised with barium carbonate. The filtered solution was evaporated almost to dryness (pale yellow crystals

separated), dilute sulphuric acid added, the filtered solution again concentrated, *S*-benzylthiuronium hydrochloride added, and the solution heated to boiling and cooled in ice. The solid *salt* was collected and recrystallised several times from water, forming pale yellow needles, m. p. 248—249° (decomp.) (Found: C, 52·1; H, 4·4; N, 7·7. $C_{28}H_{28}O_6N_4S_4$ requires C, 52·2; H, 4·4; N, 8·7%).

Action of Lead Tetra-acetate on Diphenylene.—A solution of diphenylene (0·30 g.) and lead tetra-acetate (0·90 g.) in acetic acid (15 c.c.; distilled from potassium permanganate) was heated on the steam-bath for ½ hr., cooled, and poured into water. The orange solid was collected and heated on a steam-bath with 2N-sodium hydroxide for 40 min. Filtration removed diphenylene, and the dark brown filtrate was acidified with hydrochloric acid, giving a solid which sublimed at 140°/20 mm., giving a pale yellow product (0·005 g.), m. p. 139—140° [Found (on 1·3 mg.): C, 85·1; H, 5·6. $C_{12}H_8O$ requires C, 85·7; H, 4·8%]. The compound gave an intense red colour with alcoholic ferric chloride and is probably a *hydroxydiphenylene*.

We thank Professor D. H. Hey, D.Sc., for samples of diphenyl-2-, -3-, and -4-carboxylic acid, and the Department of Scientific and Industrial Research for a maintenance allowance awarded to M. P. V. B. We acknowledge also the help of Mr. J. W. Barton in preparing diphenylene, and in particular that of Dr. R. F. Curtis in developing the improved synthesis of diphenylene described in this paper.

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The Electrophilic Reactivity of Alkoxyalkylidene Derivatives of Heterocyclic Keto-methylene Compounds.

By EDWARD B. KNOTT.

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Certain cyclic keto-methylene compounds condense with orthoesters to give 1-alkoxyalkylidene derivatives. Some of these have been converted into dimethin*mero*cyanines substituted by alkyl in the chain. 5-1′-Alkoxyalkylidenerhodanines with ammonia or primary or secondary amines give 5-1′-aminoalkylidenerhodanines. The latter were quaternized by methyl toluene-*p*-sulphonate and then converted into complex *mero*cyanines by condensation with heterocyclic keto-methylene compounds.

5-1′-Ethoxyethylidenerhodanines and 4-1′-ethoxyethylidene-2-ethylthiothiazol-5-one react with a number of thiols, to give the related alkyl(or aryl)-thioethylidene derivatives. The latter have, in many cases, been isolated in two forms believed to be the *cis*- and *trans*-isomers.

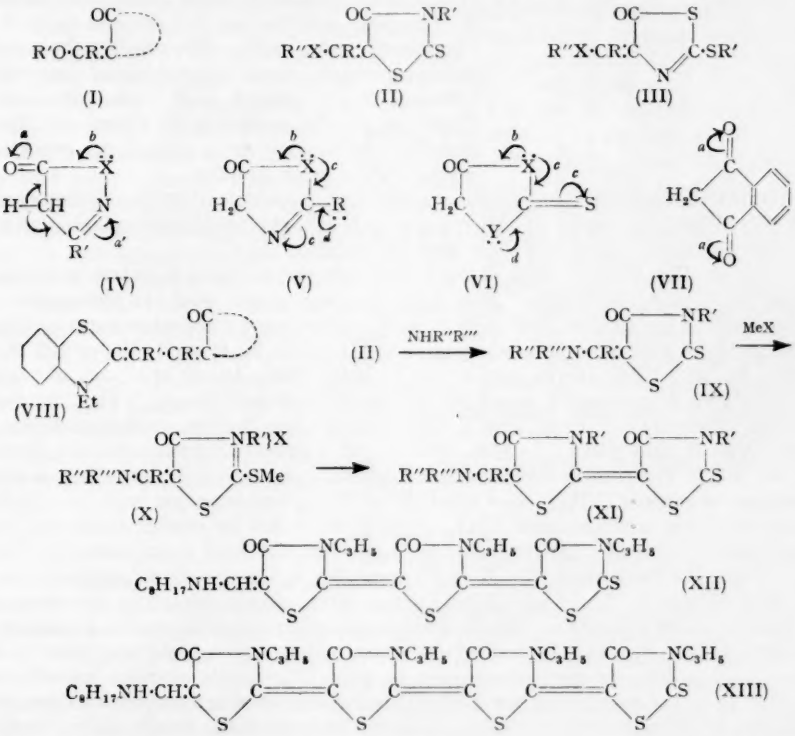
IT is known that certain heterocyclic keto-methylene compounds behave in the same way as their open-chain analogues (Claisen, *Annalen*, 1897, **297**, 5, 16; Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 4889) in forming alkoxyalkylidene derivatives (I) when refluxed with alkyl orthoesters with or without the addition of acetic anhydride. For instance, Kendall and Fry (B.P. 544,647/1940) found that pyrazolones condensed with orthoesters other than orthoformates when merely boiled together. Kendall and Duffin (B.P. 585,089, 633,736) obtained 4-alkoxyalkylidene-2-phenyloxazol-5-ones by cyclizing hippuric acid with acetic anhydride in the presence of an orthoester, and 2-alkylthio-4-ethoxymethylene- and -4-1′-ethoxyethylidene-thiazol-5-ones (III; X = O) were obtained similarly from *N*-dithioalkoxycarbonylglycines by Cook, Harris, Heilbron, and Shaw (*J.*, 1948, 1056), and by Aubert, Knott, and Williams (*J.*, 1951, 2185) respectively. Behringer and Weissauer (*Chem. Ber.*, 1952, **85**, 774) have also recently obtained 3-ethoxyalkylidene derivatives of oxindole and its *N*-acetyl derivative. These substances are useful as intermediates for *mero*cyanines, and it was therefore of interest to extend this reaction to other keto-methylene compounds, as well as to examine their reactivities towards simple nucleophilic reagents.

The nucleophilic reactivity of the methylene carbon atom of these heterocyclic compounds towards orthoesters (or aldehydes) results from the $+M$ effect of the adjacent carbonyl oxygen atom denoted in (IV) and (VII) by the curved arrow (*a*). This reactivity

is affected profoundly by the configuration of the rest of the molecule, and is enhanced by the presence of a second conjugated $+M$ atom (effect *a'*) as in pyrazolones (IV; X = NR), *iso*oxazolones (IV; X = O), and indanedione (VII). This is shown by the ability of all three of these compounds to react rapidly with boiling orthoester without the addition of acetic anhydride (cf. Kendall and Fry, *loc. cit.*).

On the other hand, in many compounds the $+M$ effect is partially neutralized by the $-M$ effect (arrow *b*) of an adjacent atom X in (IV), (V), and (VI). Whereas 3-alkyl-2-thiothiazolid-5-ones (VI; X = S, Y = NR) condense with ethyl orthoformate in acetic anhydride, the related 1 : 3-dialkyl-2-thiohydantoins (VI; X = Y = NR) are inert. The lower $-M$ effect when X = S compared with that when X = NR indicated by this difference in reactivity is in agreement with the accepted relative values.

The deactivating effect (*b*) in many of these rings is itself opposed by the activating effect of a second $+M$ atom, *e.g.*, the imino-nitrogen atom of (V) or the thione-sulphur atom in (VI), as denoted by the curved arrows (*c*). Although this effect has not been noted



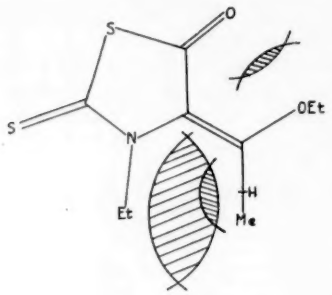
in this series it is clearly shown by the very much greater reactivity towards aldehydes of 2-thiohydantoins (VI; X = Y = NR) compared with that of the related hydantoins (Wheeler and Brautlecht, *Amer. Chem. J.*, 1911, **45**, 446), corresponding with the much weaker $+M$ effect of ketonic oxygen compared with that of thionic sulphur.

Finally there is usually a secondary deactivating process (*d*) resulting from the presence of a second $-M$ atom, *e.g.*, Y in (VI). This is shown by the fact that the replacement of Y = S by Y = O or Y = NR in (VI; X = NR), *i.e.*, an increase in this $-M$ effect, is sufficient to prevent reaction with orthoesters.

This resonance or electronic analysis of keto-methylene compounds has been described by Brooker *et al.* (*J. Amer. Chem. Soc.*, 1951, **73**, 5332) in explaining the variations in $+M$ effect (acidity) of a number of such nuclei. That an increase in the $+M$ effect

increases the nucleophilic reactivity of the nucleus was also observed in certain cases by the above authors in their experiments on oxonol formation.

Steric effects are also of importance in reactions involving orthoesters other than orthoformates when the two atoms adjacent to the reactive methylene group carry substituents. In such molecules the groups OR′ and R of the side chain which is introduced on reaction cannot lie in the same plane as the heterocyclic ring, as can be seen from scale drawings. This effect is shown by 3-ethyl-2-thiothiazolid-5-one (VI; X = S, Y = NEt) which condenses with ethyl orthoformate in acetic anhydride to give the planar 4-ethoxymethylene derivative (see Figure) but does not condense with ethyl orthoacetate. The 4-1′-ethoxyethylidene derivative which could be formed is non-planar, according to the Figure. Similar steric considerations apply to pyrazolones (IV; X = NR), *iso*oxazolones (IV; X = O), indane-1 : 3-dione (VII), and 1 : 3-disubstituted 2-thiohydantoins (VI; X, Y = NR), and the fact that the first three of these compounds react easily with ethyl orthoacetate or orthopropionate is another indication of the activating influence of the second $+M$ atom. However the distortion in the molecules is shown by their instability, decomposition occurring on repeated recrystallization or on keeping.



Attempts to condense ethyl orthobenzoate with 3-ethoxycarbonylmethylrhodanine in acetic anhydride gave traces of the required 5-1′-ethoxybenzylidenerhodanine after prolonged heating under reflux, but these were not isolated.

It is known that the $C_{(1')}$-atom of the 1-alkoxyalkylidene chain of examples of this type exhibits electrophilic reactivity. They have been condensed, with the elimination of the alkoxy-group as an alkanol, with heterocyclic quaternary salts containing a nucleophilic methyl group to give dimethin*mero*cyanines (VIII; R = H, R′ = H, Me, or Et) (Kendall and Fry, *loc. cit.*; Cook, Harris, and Shaw, *J.*, 1949, 1435; Aubert *et al.*, *loc. cit.*) and with amines to give 4-aminomethyleneoxazol-5-ones (Barber and Slack, " The Chemistry of Penicillin," Oxford Univ. Press, p. 817), 4-aminomethylene-2-mercaptothiazol-5-ones (Cook Harris, Pollock, and Swan, *J.*, 1950, 1947), and 3-aminomethyleneoxindoles (Behringer *et al.*, *loc. cit.*). The present intermediates have also been converted into chain-substituted dimethin*mero*cyanines (VIII; R = alkyl, R′ = H) by condensation with 2-methylbenzothiazole ethiodide, and also into (VIII; R = H, R′ = Me) by condensation with 2-ethylbenzothiazole ethiodide. Analogous dyes were also obtained from 2-ethylthiazolinium salts. From the rhodanines (II; X = O) numerous 4-1′-aminoalkylidenerhodanines (IX) have been obtained. These are all pale yellow dyes, closely related to the *mero*cyanines and sensitize silver chloride or chlorobromide emulsions moderately well. By analogy with the oxonols, these dyes may be termed oxamines. They are readily quaternized by methyl toluene-*p*-sulphonate or methyl sulphate to give (X), which contains an electrophilic $C_{(2)}$-atom as in the case of simpler 2-alkylthio-derivatives of heterocyclic quaternary salts. Treatment of (X) with keto-methylene heterocycles in alcoholic triethylamine leads to the more complex dyes (*e.g.*, XI). In one case the process of quaternization and condensation was repeated, to give dyes (XII) and (XIII), which are related to the complex *mero*cyanines of Kendall and Fry (B.P. 489,335) and Brooker (Mees, " The Theory of the Photographic Process," Macmillan, New York, 1942, p. 1038—1040).

Attempts to quaternize the alkoxyalkylidene derivatives (II; X = O) of 3-substituted rhodanines themselves were unsuccessful. This observation, together with the fact that the aminoalkylidene derivatives quaternize much less rapidly than related *mero*cyanines in which R″R‴N·CR: is part of a heterocyclic ring, agrees with the expectation that the rate of quaternization would increase with an increase in the electron density on the thionic sulphur atom, since this is the point of attack by the electrophilic methyl group of methyl toluene-*p*-sulphonate. The process denoted by arrow (*c*) in (VI) would thus be an activating process for quaternization. Deactivation, represented by the arrow (*b*), is a

result of the presence of the carbonyl-oxygen atom and will be decreased by any $-M$ effect from the group in the 5-position which will tend to satisfy the $+M$ effect of the carbonyl-oxygen atom. Such a $-M$ effect increases in the order: ethoxyalkylidene, amino-alkylidene, nitrogen-heterocyclidene, as is known from other data.

For certain reactions described in the following paper and involving the nucleophilic reactivity of the $C_{(2)}$-atom of the ethylidene group (I; R = Me), 1'-alkyl(aryl)thioethylidene derivatives (*e.g.*, II or III; X = S, R = Me) were required. Condensation of the keto-methylene compound with ethyl trithio-orthoformate did not proceed as expected. Croxall, Freimuller, and Shropshire (*J. Amer. Chem. Soc.*, 1950, **72**, 4275) obtained β-arylthio-acrylates by heating β-ethoxyacrylates with thiophenol, etc., in the presence of sodium hydrogen sulphate; Cook *et al.* (*loc. cit.*, 1950) condensed toluene-ω-thiol with 4-ethoxy-methylene-2-mercaptothiazol-5-one with triethylamine as catalyst; and Behringer *et al.* (*loc. cit.*) obtained alkylthio- and arylthio-methyleneoxindoles by fusion of ethoxy-methyleneoxindole with the required thiol. A similar method which gave high yields of the required compounds was to treat 5-1'-ethoxyethylidenerhodanine (II; X = O) or 4-1'-ethoxyethylidene-2-ethylthiothiazol-5-one (III; X = O) at room temperature with the required thiol in the presence of zinc chloride and hydrogen chloride. In this way the ethylthio-, *iso*propylthio-, *n*-butylthio-, *n*-octylthio-, benzylthio-, and *p*-tolylthio-groups were introduced. [Attempts to bring about the reaction of two molecules of (I) with ethanedithiol and toluene-3 : 4-dithiol were unsuccessful.] In most cases the product was isolated in two forms differing considerably in melting point. These are believed to be *cis*- and *trans*-isomers. Related isomers were isolated by Cook *et al.* (*loc. cit.*, 1950). Similarly *cis*- and *trans*-arylthioacrylates were obtained by Croxall *et al.* (*loc. cit.*), but Behringer *et al.* (*loc. cit.*) could not isolate such isomers of 3-arylthiomethyleneoxindole. That no such geometrical isomers have been isolated in the case of 1'-ethoxyethylidene derivatives is possibly due to the stronger $-M$ effect of the OR compared with the SR group. The resultant decrease in the bond order of the double bond in the side chain would tend to make the existence or isolation of the form with higher energy less likely. Lur'e and Ravdel (*Doklady Akad. Nauk S.S.S.R.*, 1952, **83**, 97) have, however, isolated stereoisomers of 4-1'-ethoxyethylidene-2-phenyloxazol-5-one. Similar considerations apply to the strongly resonating dimethin*mero*cyanines prepared from these intermediates, both forms of the latter giving the same dye.

These arylthioethylidene or alkylthio-derivatives all exhibit the electrophilic reactivity characteristic of the alkoxyethylidene analogues.

Experimental

Determinations of $\lambda_{max.}$ are in MeOH unless otherwise stated.

4-1'-Ethoxyethylidene-2-ethylthiothiazol-5-one (III; R = Me, R', R'' = Et, X = O).—*N*-Dithioethoxycarbonylglycine (108 g.), ethyl orthoacetate (200 c.c.), and acetic anhydride (400 c.c.) were heated together on the steam-bath for 1 hr. (or at 125° in an oil-bath for 30 min.). The solvents were removed and the residual oil was distilled. The distillate (b. p. 124—140°/2 mm.) was redistilled and collected at 132—134°/2 mm. It (76·25 g., 55%) formed an orange oil which partly solidified to long needles at 4° (Found: C, 47·1; H, 5·5; N, 6·2; S, 27·5. $C_9H_{13}O_2NS_2$ requires C, 46·8; H, 5·6; N, 6·05; S, 27·7%).

2-Benzylthio-4-1'-ethoxyethylidenethiazol-5-one (III; R = Me, R''X = EtO, R' = CH_2Ph) was obtained similarly from *N*-dithiobenzyloxycarbonylglycine in 32% yield. It distilled as an orange oil, b. p. 208°/1 mm. (Found: S, 21·95. $C_{14}H_{15}O_2NS_2$ requires S, 21·85%).

2-1'-Ethoxyethylideneindane-1 : 3-dione.—Indane-1 : 3-dione (2·9 g.) and ethyl orthoacetate (10 c.c.) were refluxed together for 3 min. The product separated as a crystalline mass. After chilling, the crystals were collected, and formed brown needles, m. p. 151—158°, from ethanol. It tended to decompose on recrystallization (Found: C, 72·1; H, 5·4. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·55%).

4-1'-Ethoxyethylidene-3-phenylisooxazol-5-one.—Obtained similarly in 63% yield after boiling the reactants for 5 min., this *compound* formed pale brown plates, m. p. 113°, from ethanol (Found: C, 67·4; H, 5·65; N, 6·35. $C_{13}H_{13}O_3N$ requires C, 67·6; H, 5·65; N, 6·15%). It decomposed during 24 hr. at room temperature.

3-Ethoxycarbonylmethyl-5-ethoxymethylene-2-thiothiazolid-4-one (II; R = H, R' =

$CH_2{\cdot}CO_2Et$, R″X = EtO).—3-Ethoxycarbonylmethylrhodanine (30 g.), ethyl orthoformate (75 c.c.), and acetic anhydride (120 c.c.) were cautiously heated together until reaction set in. When this slackened the whole was refluxed for 1 hr., the solvent was distilled off, and the residue dissolved in hot *iso*propanol (50 c.c.). The substance obtained on chilling of the *iso*propanol solution formed pale yellow needles, m. p. 100—101°, in 80·5% yield after a further recrystallization from the same solvent (Found: C, 43·65; H, 5·05; N, 5·0; S, 23·1. $C_{10}H_{13}O_4NS_3$ requires C, 43·65; H, 4·75; N, 5·1; S, 23·3%).

3-*Ethoxycarbonylmethyl*-5-1′-*ethoxyethylidene*-2-*thiothiazolid*-4-*one* (II; R = Me, R′ = $CH_2{\cdot}CO_2Et$, R″X = EtO).—3-Ethoxycarbonylmethylrhodanine (87·6 g.), ethyl orthoacetate (150 c.c.), and acetic anhydride (500 c.c.), in a 1½-l. flask with a reflux condenser, were heated cautiously on a gauze. An exothermic reaction occurred and was controlled by cooling. After the initial reaction had slackened, the mixture was refluxed for 1 hr., the solvents were removed under reduced pressure, and the residual *product* recrystallized from ligroin. It (93·0 g., 80·5%) formed flat, buff needles, m. p. 105°, after a second recrystallization from *iso*propanol (Found: N, 4·9; S, 22·3. $C_{11}H_{15}O_4NS_3$ requires N, 4·85; S, 22·1%), $\lambda_{max.}$ 352 mμ.

4-*Ethoxymethylene*-3-*ethyl*-2-*thiothiazolid*-5-*one*.—3-Ethyl-2-thiothiazolid-5-one (Jeffreys and Knott, *J.*, 1952, 4632) (1·0 g.), ethyl orthoformate (2 c.c.), and acetic anhydride (5 c.c.) were heated together on a steam-bath for 30 min. Removal of the solvents left a brown oil from which the required *product* was extracted with ligroin (b. p. 100—120°). It formed colourless needles, m. p. 76°, after a further recrystallization from ligroin (Found: S, 29·6. $C_8H_{11}O_2NS_3$ requires S, 29·5%).

Further examples of this type are given in Table 1.

2-[1-(3-*Ethylbenzothiazolin*-2-*ylidene*)*prop*-2-*ylidene*]*indane*-1 : 3-*dione* (cf. VIII; R = Me, R′ = H).—2-Methylbenzothiazole ethiodide (1·5 g.), 2-1′-ethoxyethylideneindane-1 : 3-dione (1·1 g.), ethanol (20 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 5 min. The whole solidified rapidly and the dye was obtained in 82% yield as soft red needles, m. p. 270° (decomp.), from benzene–ethanol (Found: C, 72·35; H, 4·95. $C_{21}H_{17}O_2NS$ requires C, 72·6; H, 4·9%), $\lambda_{max.}$ 496 mμ.

4-[1-(3-*Ethylbenzothiazolin*-2-*ylidene*)*prop*-2-*ylidene*]-3-*phenylisooxazol*-5-*one* (cf. VIII; R = Me, R′ = H).—Obtained similarly from 4-1′-ethoxyethylidene-3-phenyl*iso*oxazol-5-one (1·15 g.) in 72% yield, the *dye* formed orange-red needles, m. p. 203°, from benzene–ethanol (Found: N, 8·0; S, 8·9. $C_{21}H_{18}O_2N_2S$ requires N, 7·75; S, 8·85%), $\lambda_{max.}$ 477 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)*prop*-2-*ylidene*]-2-*thiothiazolid*-4-*one* (cf. VIII; R = Me, R′ = H).—Obtained similarly from 3-ethoxycarbonylmethyl-5-1′-ethoxyethylidenerhodanine (1·45 g.), the *dye* (67% yield) formed soft, brown needles, m. p. 176°, from pyridine–ethanol (Found: N, 6·5; S, 22·7. $C_{19}H_{20}O_3N_2S_3$ requires N, 6·65; S, 22·9%), $\lambda_{max.}$ 530 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)*but*-2-*ylidene*]-2-*thiothiazolid*-4-*one* (cf. VIII; R = Et, R′ = H).—2-Methylbenzothiazole ethiodide (1·5 g.), 3-ethoxycarbonylmethyl-5-1′-ethoxypropylidenerhodanine (1·45 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 15 min. When the mixture was chilled, the *dye* separated as an oil which crystallized on being scratched. It (1·7 g., 78·5%) formed a green crystalline powder, m. p. 182°, from benzene–ethanol (Found: N, 6·5; S, 21·95. $C_{20}H_{22}O_3N_2S_3$ requires N, 6·45; S, 22·15%), $\lambda_{max.}$ 530 mμ.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylbenzothiazolin*-2-*ylidene*)*prop*-1-*ylidene*]-2-*thiothiazolid*-4-*one* (cf. VIII; R = H, R′ = Me).—2-Ethylbenzothiazole ethiodide (1·6 g.), 3-ethoxycarbonylmethyl-4-ethoxymethylenerhodanine (1·4 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 15 min. The *dye* (0·8 g., 38%), collected after chilling of the mixture for 3 hr., formed fine, dark red needles, m. p. 159°, from benzene–ethanol (Found: N, 6·45; S, 23·0. $C_{19}H_{20}O_3N_2S_3$ requires N, 6·65; S, 22·9%), $\lambda_{max.}$ 530 mμ.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylthiazolidin*-2-*ylidene*)*prop*-1-*ylidene*]-2-*thiothiazolid*-4-*one* was obtained similarly from 2-ethylthiazoline ethiodide (1·35 g.) in 50% yield and formed flat, magenta needles, m. p. 121°, from ethanol (Found: N, 7·75; S, 25·6. $C_{15}H_{20}O_3N_2S_3$ requires N, 7·55; S, 25·8%), $\lambda_{max.}$ 490 mμ.

4-[2-(3-*Ethylbenzothiazolin*-2-*ylidene*)*prop*-1-*ylidene*]-2-*ethylthiothiazol*-5-*one* (cf. VIII; R = H, R′ = Me).—2-Ethylbenzothiazole ethiodide (1·6 g.), 4-ethoxymethylene-2-ethylthiothiazol-5-one (1·1 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 10 min. The *dye* (0·9 g., 50%) obtained on chilling formed red flakes with a blue reflex, m. p. 112°, from ethanol. The crystals lost ethanol in a vacuum-desiccator (Found: N, 7·7; S, 26·3. $C_{17}H_{18}ON_2S_3$ requires N, 7·75; S, 26·5%), $\lambda_{max.}$ 540 mμ.

TABLE 1. *3-Substituted 4-1'-alkoxyalkylidene-2-thiothiazolid-4-ones* (II; X = O).

R	R'	R''	Reaction time (min.)	Yield (%)	Appearance (solvent) †	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Found (%) S	Required (%) C	Required (%) H	Required (%) N	Required (%) S
Me	Et	Et	240	51	Orange needles (P)	80°	$C_9H_{13}O_2NS_2$	—	—	5·95	27·8	—	—	6·05	27·7
Me	Ph	Et	45	93·5	Orange needles (M)	164—166	$C_{13}H_{13}O_2NS_2$	55·2	4·9	—	23·25	55·5	4·65	—	22·9
H	Ph	Et	60	73	Cream needles (E)	150—151	$C_{12}H_{11}O_2NS_2$	—	—	5·55	24·05	—	—	5·3	24·2
Et	Ph	Et	60	22	Orange plates (P)	180—182	$C_{14}H_{15}O_2NS_2$	56·8	5·05	4·85	21·55	57·3	5·1	4·8	21·85
H	A *	Et	300	69·5	Red needles (A)	53—54	$C_9H_{11}O_2NS_2$	47·7	5·15	6·25	27·9	47·2	4·8	6·1	27·95
Me	A *	Et	300	88·5	Brown plates (L)	63—64	$C_{10}H_{13}O_2NS_2$	49·6	5·5	5·65	26·2	49·4	5·35	5·75	26·35
Et	A *	Et	480	55	Gold needles (P)	62—63	$C_{11}H_{15}O_2NS_2$	—	—	5·35	—	—	—	5·45	—
Me	A *	Me	600	44·5	Brown needles (P)	83—84	$C_9H_{11}O_2NS_2$	—	—	6·15	27·95	—	—	6·1	27·95
Me	C *	Me	60	97·5	Straw needles (P)	113—114	$C_{10}H_{13}O_4NS_2$	43·85	4·85	—	22·95	43·6	4·7	—	23·3
H	B *	Et	300	74·5	Pink needles (P)	87	$C_{13}H_{13}O_2NS_2$	—	—	4·95	—	—	—	5·0	—
Me	B *	Et	300	59	Flat needles (P)	109	$C_{14}H_{15}O_2NS_2$	—	—	4·7	22·1	—	—	4·8	22·0
H	CH *	Et	150	50	Yellow needles (P)	139—140	$C_{12}H_{17}O_2NS_2$	—	—	4·9	23·7	—	—	5·15	23·6
Me	CH *	Et	180	59	Orange flakes (P)	105	$C_{13}H_{19}O_2NS_2$	—	—	4·7	22·1	—	—	4·9	22·45

* A = allyl, B = benzyl, C = ethoxycarbonylmethyl, CH = *cyclo*hexyl.
† E = ethanol; M = methanol; A = *cyclo*hexane; P = *iso*propanol; L = light petroleum, b. p. 60—80°.

TABLE 2. *3-Substituted 5-1'-aminoalkylidene-2-thiothiazolid-4-ones.*

R	R''R'''N	Yield (%)	Appearance	M. p.	Formula	Found (%) N	Found (%) S	Required (%) N	Required (%) S
	(IX; R' = $CH_2{\cdot}CO_2Et$)								
Me	Anilino	79·5	Golden laths	173—175°	$C_{15}H_{16}O_3N_2S_2$	8·15	19·1	8·35	19·05
H	Piperidyl	76·5	Pale yellow needles	146—147	$C_{13}H_{18}O_3N_2S_2$	8·8	20·6	8·9	20·4
H	Morpholinyl	95·0	Flat yellow needles	172—173	$C_{12}H_{16}O_4N_2S_2$	8·6	—	8·85	—
H	*N*-Methylanilino	41·5	Orange laths	146—149	$C_{15}H_{16}O_3N_2S_2$	8·15	—	8·35	—
H	Benzylamino	62·5	Yellow needles	109	$C_{15}H_{16}O_3N_2S_2$	8·3	—	8·35	—
H	β-Phenylhydrazino	65	Straw needles	184	$C_{14}H_{15}O_3N_3S_2$ [d]	12·3	18·75	12·45	19·0
H	*cyclo*Hexylamino	70	Yellow tablets	133—134	$C_{14}H_{20}O_3N_2S_2$	8·3	—	8·55	—
Me	Ethylamino	95	Cream plates	121	$C_{11}H_{16}O_3N_2S_2$	9·7	—	9·7	—
H	Dibenzylamino	94	Yellow needles	103—104	$C_{22}H_{22}O_3N_2S_2$	6·5	—	6·55	—
H	Di*cyclo*hexylamino	73	Yellow tablets	159	$C_{20}H_{30}O_3N_2S_2$	6·7	—	6·85	—
	(IX; R' = $CH_2{\cdot}CH{:}CH_2$)								
H	Amino	90	Orange needles [a]	104—109	$C_7H_8ON_2S_2$	13·8	—	14·0	—
H	Carboxymethylamino [b]	90	Yellow needles	195—196	$C_9H_{10}O_3N_2S_2$	10·65	—	10·85	—
Me	Ethylamino	93	Straw flakes	65	$C_{10}H_{14}ON_2S_2$	11·7	26·3	11·55	26·45
H	Morpholinyl	85	Yellow needles [c]	180	$C_{11}H_{14}O_2N_2S_2$	10·1	—	10·35	—
H	Diethylamino	67	Yellow needles	74	$C_{11}H_{16}ON_2S_2$ [e]	10·75	—	10·95	—
Et	Ethylamino	70	Orange flakes	49—51	$C_{11}H_{16}ON_2S_2$	10·8	—	10·95	—
H	*n*-Octylamino	92	Yellow threads	98—100	$C_{15}H_{24}ON_2S_2$ [f]	9·0	20·4	9·0	20·5
H	Ethylamino	88	Yellow threads	132	$C_9H_{12}ON_2S_2$	12·25	28·2	12·3	28·1

[a] From aq. ethanol. [b] Obtained from the potassium salt of glycine. [c] From benzene. [d] Found: C, 50·25; H, 4·25. Reqd.: C, 49·8; H, 4·45%.
[e] Found: C, 51·7; H, 6·05. Reqd.: C, 51·55; H, 6·25%. [f] Found: C, 57·4; H, 7·75. Reqd.: C, 57·7; H, 7·7%.

2-*Ethylthio*-4-[2-(3-*methylthiazolidin*-2-*ylidene*)*prop*-1-*ylidene*]*thiazol*-5-*one*, obtained (0·8 g., 52·5%) similarly from 2-ethylthiazoline methiodide (1·3 g.), formed orange rosettes, m. p. 119°, from ethanol (Found: N, 9·35. $C_{12}H_{16}ON_2S_3$ requires N, 9·35%), $\lambda_{max.}$ 490 mμ.

3-*Substituted* 5-1′-*aminoalkylidene*-2-*thiothiazolid*-4-*ones* (IX) (Table 2) were all obtained by heating equimolecular amounts of (II; X = O) and the amine in ethanol on a steam-bath for 15—30 min. They usually crystallized when the liquid was chilled, and were recrystallized from ethanol unless otherwise stated.

1 : 6-*Di*-(3-*ethoxycarbonylmethyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-2 : 5-*diazahexane*.—3-Ethoxycarbonylmethyl-5-ethoxymethylenerhodanine (5·5 g.), ethylenediamine hydrate (0·81 c.c.), and ethanol (25 c.c.) were refluxed together for 15 min. When the resulting solution was chilled a thick oil separated which solidified on being scratched. From ethanol (twice) it (3·6 g., 70%) formed pale yellow needle agregates, m. p. 145° (Found: N, 10·75; S, 24·5. $C_{18}H_{22}O_6N_4S_4$ requires N, 10·8; S, 24·7%).

5-*Benzothiazol*-2′-*ylaminomethylene*-3-*ethoxycarbonylmethyl*-2-*thiothiazolid*-4-*one*.—3-Ethoxycarbonylmethyl-5-ethoxymethylenerhodanine (2·75 g.), 2-aminobenzothiazole (1·5 g.), and ethanol (10 c.c.) were refluxed together for 1 hr. The *compound* separated on chilling and formed yellow needles, (2·65 g., 70%), m. p. 190—191°, from ethanol (Found: N, 10·95. $C_{15}H_{13}O_3N_3S_3$ requires N, 11·1%).

3-*Ethoxycarbonylmethyl*-5-(3-*ethylbenzothiazolin*-2-*ylideneaminomethylene*)-2-*thiothiazolid*-4-*one*.—This dye was prepared as in the preceding preparation, with 2-aminobenzothiazole ethotoluene-*p*-sulphonate (3·5 g.) and triethylamine (1·5 c.c.). The *product* (3·2 g., 79%) was obtained as orange plates, m. p. 199°, from benzene (Found: N, 10·55. $C_{17}H_{17}O_3N_3S_3$ requires N, 10·35%).

3-*Allyl*-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)-5-n-*octylaminomethylenethiazolid*-4-*one*.—3-Allyl-5-*n*-octylaminomethylenerhodanine (0·8 g.) and methyl toluene-*p*-sulphonate (0·5 g.) were fused together at 150° for 2 hr. *N*-Dithioethoxycarbonylglycine (1·0 g.) was cyclized to 2-ethylthiothiazol-5-one by heating it with acetic anhydride (20 c.c.) for 1 hr. on a steam-bath. The solvent was removed and the residual oil washed into the above quaternary salt with ethanol (10 c.c.). Triethylamine (1·0 c.c.) was added and the whole heated for 5 min. on the steam-bath. The yellow needles (0·3 g., 27%) which separated on chilling formed soft yellow threads, m. p. 156°, from ethanol (Found: N, 9·75; S, 22·0. $C_{20}H_{29}O_2N_3S_3$ requires N, 9·95; S, 21·9%), $\lambda_{max.}$ 450 mμ.

3-*Ethoxycarbonylmethyl*-2-(3-*ethyl*-4-*oxo*-2-*thio-oxazolidin*-5-*ylidene*)-5-*morpholin*-3′-*ylmethylenethiazolid*-4-*one*.—3-Ethoxycarbonylmethyl-5-morpholin-3′-ylmethylenerhodanine (1·0 g.) and methyl toluene-*p*-sulphonate (0·6 g.) were fused together at 125° for 1 hr. 3-Ethyl-2-thiooxazolid-4-one (0·5 g.), ethanol (10 c.c.), and triethylamine (0·5 c.c.) were added and the mixture was refluxed for 10 min. The yellow grains (0·5 g., 37%) obtained when the resulting product was chilled formed yellow needles, m. p. 155—157°, from *iso*propanol (Found: N, 10·0. $C_{17}H_{21}O_6N_3S_2$ requires N, 9·85%), $\lambda_{max.}$ 418 mμ.

[3-*Allyl*-4-*oxo*-5-n-*octylaminomethylene*-2-*thiazoline*][3-*ethyl*-2-*benzothiazole*]*methincyanine Perchlorate*.—3-Allyl-5-*n*-octylaminomethylenerhodanine (0·8 g.) and methyl toluene-*p*-sulphonate were fused for 2 hr. at 140°. 2-Methylbenzothiazole ethotoluene-*p*-sulphonate (0·9 g.), ethanol (10 c.c.), and triethylamine (0·4 c.c.) were added and the mixture was refluxed for 10 min. Saturated aqueous sodium perchlorate (0·5 c.c.) was added and the flask chilled overnight. The *dye* (0·9 g., 63·5%) formed light brown threads, m. p. 190°, from ethanol (Found: N, 7·65; S, 11·6. $C_{25}H_{34}O_5N_3ClS_2$ requires N, 7·55; S, 11·55%), $\lambda_{max.}$ 465 mμ.

2-*Dicyanomethylene*-3-*ethoxycarbonylmethyl*-5-*piperid*-1′-*ylmethylenethiazolid*-4-*one*.—3-Ethoxycarbonylmethyl-5-piperid-1′-ylmethylenerhodanine (1·6 g.) was quaternized as above and refluxed for 15 min. with malononitrile (0·4 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.). The *dye* (0·6 g., 34%) formed pale yellow crystals, m. p. 164—166°, after three recrystallizations from ethanol (Found: N, 16·0. $C_{16}H_{18}O_3N_4S$ requires N, 16·2%), $\lambda_{max.}$ 386 mμ.

3-*Allyl*-2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-5-*ethylaminomethylenethiazolid*-4-*one* (XI; R, R″ = H, R′ = allyl, R‴ = Et).—3-Allyl-5-ethylaminomethylenerhodanine (2·3 g.) and methyl toluene-*p*-sulphonate were fused at 130° for 2 hr. 3-Allylrhodanine (1·8 g.), ethanol (10 c.c.), and triethylamine (1·5 c.c.) were added and heated for 5 min. on a steam-bath. The *dye* (2·65 g., 72%) formed orange flakes, m. p. 177°, from ethanol (Found: N, 11·5. $C_{15}H_{17}O_2N_3S_3$ requires N, 11·45%), $\lambda_{max.}$ 459 mμ in EtOH.

5-N-*Acetylethylamidomethylene*-3-*allyl*-2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)*thiazolid*-4-*one* (XI; R = H, R′ = allyl, R″ = Ac, R‴ = Et).—The previous dye (1·0 g.) and acetic anhydride (25 c.c.) were refluxed together for 3 hr. and the solvents were removed. The residual *product*

formed long, orange-brown needles (0·8 g.), m. p. 160—161°, after two recrystallizations from ethanol (Found: C, 50·1; H, 4·75; N, 10·3; S, 23·2. $C_{17}H_{19}O_3N_3S_2$ requires C, 49·85; H, 4·65; N, 10·3; S, 23·45%), $\lambda_{max.}$ 441 mμ.

3-*Ethoxycarbonylmethyl*-2-(3-*ethoxycarbonylmethyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-5-*piperid*-1′-*ylmethylenethiazolid*-4-*one* (XI; R′ = CH_2·CO_2Et, R = H, R″R‴N = piperidyl).—3-Ethoxycarbonylmethyl-5-1′-piperidinomethylene-2-thiothiazolid-4-one (1·6 g.) and methyl toluene-*p*-sulphonate (0·95 g.) were fused together for 2 hr. at 120°. 3-Ethoxycarbonylmethylrhodanine (1·1 g.), ethanol (20 c.c.), and triethylamine were added and the whole was refluxed for 5 min. on a steam-bath. A solid yellow mass of crystals separated. They were washed with ethanol and formed soft, yellow needle rosettes (1·5 g., 59·0%), m. p. 234°, from benzene–ethanol (Found: N, 8·4; S, 19·2. $C_{20}H_{25}O_5N_3S_3$ requires N, 8·45; S, 19·2%), $\lambda_{max.}$ 458 mμ.

3-*Allyl*-2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-5-n-*octylaminomethylenethiazolid*-4-*one* (XI; R, R″ = H, R‴ = *n*-octyl R′ = allyl).—Obtained similarly in 62% yield, this *dye* formed orange flakes, m. p. 127—128°, from methanol (Found: N, 9·3; S, 21·15. $C_{21}H_{29}O_2N_3S_3$ requires N, 9·3; S, 21·3%), $\lambda_{max.}$ 460 mμ.

3-*Allyl*-2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-5-(3-*allyl*-4-*oxo*-5-n-*octylaminomethylene*-*thiazolidin*-2-*ylidene*)*thiazolid*-4-*one* (XII).—The preceding dye (XI) (1·5 g.) and methyl toluene-*p*-sulphonate (0·65 g.) were fused at 130° for 1 hr. 3-Allylrhodanine (0·6 g.), ethanol (15 c.c.), and triethylamine (0·5 c.c.) were added and the whole was refluxed for 5 min. The *dye* (1·25 g., 63·5%) which separated on chilling formed soft, red needles, m. p. 199—201°, from benzene–ethanol (Found: N, 9·3; S, 21·8. $C_{27}H_{34}O_3N_4S_4$ requires N, 9·5; S, 21·7%), $\lambda_{max.}$ 508 mμ in MeOH, 518 mμ in pyridine.

3-*Allyl*-2-[3-*allyl*-2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-4-*oxothiazolidin*-5-*ylidene*]-5-(3-*allyl*-4-*oxo*-5-n-*octylaminomethylenethiazolidin*-2-*ylidene*)*thiazolid*-4-*one* (XIII).—The above dye (0·7 g.) and methyl toluene-*p*-sulphonate (0·5 g.) were fused at 140° for 30 min. To the solid quaternary salt were added 3-allylrhodanine (0·25 g.) and ethanol (20 c.c.), and the mixture was heated to give a red solution. Triethylamine (0·3 c.c.) was then added to give an immediate precipitation of the *dye*, which (0·6 g., 70%) formed a red crystalline powder, m. p. 263°, from pyridine (Found: C, 54·1; H, 5·3; N, 9·5; S, 22·1. $C_{33}H_{39}O_4N_5S_5$ requires C, 54·3; H, 5·35; N, 9·6; S, 21·95%), $\lambda_{max.}$ 548 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-5-1′-*ethylthioethylidene*-2-*thiothiazolid*-4-*one* (II; R = Me, R″X = EtS, R′ = CH_2·CO_2Et).—3-Ethoxycarbonylmethyl-5-1′-ethoxyethylidenerhodanine (2·9 g.), ethanethiol (1·5 c.c.), powdered anhydrous zinc chloride (2·7 g.), and dioxan (10 c.c.) were saturated with dry hydrogen chloride at 25° and set aside for 15 hr. Water (100 c.c.) was added to precipitate an orange oil which soon solidified. From ethanol this *compound* (2·8 g., 82%) formed yellow flakes, m. p. 67—68° (Found: C, 43·55; H, 5·15; N, 4·75; S, 31·2. $C_{11}H_{15}O_3NS_3$ requires C, 43·25; H, 4·9; N, 4·6; S, 31·5%), $\lambda_{max.}$ 370 mμ.

3-*Ethoxycarbonylmethyl*-5-1′-iso*propylthioethylidene*-2-*thiothiazolid*-4-*one* was obtained in 54·5% yield as pale yellow flakes, m. p. 107—108°, from light petroleum (b. p. 60—80°) (Found: C, 45·3; H, 5·45; N, 4·5; S, 29·9. $C_{12}H_{17}O_3NS_3$ requires C, 45·1; H, 5·35; N, 4·4; S, 30·3%).

5-1-n-*Butylthioethylidene*-3-*ethoxycarbonylmethyl*-2-*thiothiazolid*-4-*one* was obtained similarly from *n*-butanethiol in 82·5% yield and formed pale yellow tablets, m. p. 68—69° (Found: C, 47·05; H, 5·8; N, 4·15; S, 28·8. $C_{13}H_{19}O_3NS_3$ requires C, 46·85; H, 5·7; N, 4·2; S, 28·65%), and orange needles, m. p. 92—93°, from light petroleum (b. p. 60—80°) (Found: C, 46·9; H, 5·75; S, 29·0%). The solid with the higher m. p. crystallizes first from the solvent.

5-1′-*Benzylthioethylidene*-3-*ethoxycarbonylmethyl*-2-*thiothiazolid*-4-*one* was obtained similarly by using toluene-ω-thiol and formed pale yellow flakes, m. p. 99—100°, in 46·5% yield after three recrystallizations from ethanol (Found: S, 26·3. $C_{16}H_{17}O_3NS_3$ requires S, 26·15%), $\lambda_{max.}$ 375 mμ.

5-1′-*Ethylthioethylidene*-3-cyclo*hexyl*-2-*thiothiazolid*-4-*one*.—5-1′-Ethoxyethylidene-3-*cyclo*hexylrhodanine (14·25 g.), ethanethiol (7·5 c.c.), powdered zinc chloride (13·6 g.), and dioxan (50 c.c.) were saturated with dry hydrogen chloride at 25° and set aside for 20 hr. Water (200 c.c.) was added to precipitate a yellow oil which rapidly crystallized. The yield of crude air-dried *product* was 98·5% (14·75 g.). From light petroleum (b. p. 60—80°) yellow threads first separated (3·5 g.). After two further recrystallizations from the same solvent they had m. p. 148—149° (Found: S, 31·8. $C_{13}H_{19}ONS_3$ requires S, 31·9%), $\lambda_{max.}$ 374 mμ in MeOH. The filtrate from the first crystallization on concentration and chilling gave soft yellow needles (9·1 g.), m. p. 89—91°, from *iso*propanol (Found: S, 32·1), $\lambda_{max.}$ 374 mμ.

3-*Benzyl*-5-1′-*ethylthioethylidene*-2-*thiothiazolid*-4-*one*.—Obtained similarly from 3-benzyl-5-1′-ethoxyethylidenerhodanine, the *product* (81% yield) after one recrystallization from *iso*-

propanol was dissolved in the same solvent (30 c.c./g.) and allowed to cool. Fine orange needles (34·6%), m. p. 107—108°, after a second recrystallization, separated first (Found: C, 54·85; H, 4·65; N, 4·45; S, 30·9. $C_{14}H_{15}ONS_3$ requires C, 54·35; H, 4·85; N, 4·55; S, 31·1%); it had $\lambda_{max.}$ 376 mμ in MeOH. The filtrate then deposited pale yellow threads (48·4%), m. p. 107—108° with softening at 92° (Found: C, 54·5; H, 4·7; N, 4·4; S, 31·3%), λ_{max} 375 mμ.

3-*Ethoxycarbonylmethyl*-5-1′-p-*tolylthioethylidene*-2-*thiothiazolid*-4-*one*.—Obtained crude in 100% yield from *p*-thiocresol, the first crop from *iso*propanol (36·5% yield) formed orange flakes, m. p. 139—140°, after two recrystallizations from the same solvent (Found: C, 51·9; H, 4·8; N, 3·65; S, 25·95. $C_{16}H_{17}O_3NS_3$ requires C, 52·3; H, 4·65; N, 3·8; S, 26·2%). The second crop (43·5% yield) obtained on concentration of the first filtrate formed flat, yellow needles, m. p. 91·5°, from *iso*propanol (Found: C, 52·2; H, 4·75; N, 3·75; S, 26·35%). 3-*Allyl*-5-1′-p-*tolylthioethylidene*-2-*thiothiazolid*-4-*one* was obtained in 35% yield and formed flat, cream needles, m. p. 90°, from *iso*propanol (Found: C, 55·95; H, 4·85; N, 4·2; S, 29·95. $C_{15}H_{15}ONS_3$ requires C, 56·05; H, 4·7; N, 4·35; S, 30·0%).

3-*Ethoxycarbonylmethyl*-5-1′-n-*octylthioethylidene*-2-*thiothiazolid*-4-*one* was obtained similarly from molar amounts of reactants. The mixture was set aside for 72 hr. before addition of water. The oil was distilled and collected (54% yield) at 232—240°/2·5 mm. It slowly crystallized and a sample formed soft, pale yellow needles, m. p. 38°, from *iso*propanol (Found: S, 26·5. $C_{17}H_{27}O_3NS_3$ requires S, 26·65%).

2-*Ethylthio*-4-1′-*ethylthioethylidenethiazol*-5-*one* (III; R = Me, R′, R″ = Et, X = S).—4-1′-Ethoxyethylidene-2-ethylthiothiazol-5-one (23·1 g.) was dissolved in dioxan (30 c.c.) and ethanethiol (15 c.c.). Powdered anhydrous zinc chloride (27 g.) was added and the whole saturated at 25° with dry hydrogen chloride. The orange solution was shaken with water and ether, the ethereal layer dried (Na_2SO_4), and the ether removed. Distillation gave an orange oil, b. p. 120/3 mm. (5·45 g.), which was rejected and the required compound (16·15 g., 65%), b. p. 170°/3 mm., which solidified in the receiver. It formed pale yellow needles, m. p. 60—61°, from *iso*propanol (Found: C, 43·65; H, 5·65; N, 5·7; S, 38·75. $C_9H_{13}ONS_3$ requires C, 43·7; H, 5·25; N, 5·65; S, 38·9%), $\lambda_{max.}$ 370 mμ.

We thank Mr. C. B. Dennis of these laboratories for several microanalyses.

RESEARCH LABORATORIES, KODAK LTD.,
WEALDSTONE, MIDDLESEX.

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The Nucleophilic Reactivity of Alkylidene Derivatives of Cyclic Keto-methylene Compounds.

By EDWARD B. KNOTT.

[Reprint Order No. 4786.]

3-Substituted rhodanines have been condensed with acetaldehyde, crotonaldehyde, acetone, diacetyl, and pyruvic acid, to give 4-alkylidene derivatives. These and the 1′-alkoxy- and 1′-alkylthio-ethylidene derivatives of a number of cyclic keto-methylene compounds have been condensed with electrophilic, cyclic quaternary ammonium salts to give simple and complex *mero*cyanines and oxamines. Some of the complex dyes have their main absorption band almost completely in the infra-red region, a phenomenon which is believed to be unique for non-ionic dyes.

THE nucleophilic reactivity of the methylene carbon atom in cyclic keto-methylene compounds is shown by the formation of condensation products with aldehydes (Nencki, *Ber.*, 1884, **17**, 2277), ketones (Knorr, *Annalen*, 1887, **238**, 180), and ortho-esters (preceding paper). It is also utilized in the preparation of *mero*cyanines (II) by treating the keto-methylene compound with derivatives of heterocyclic quaternary ammonium compounds (I) containing an electrophilic carbon atom. This method is usually employed in the preparation of *mero*cyanines and higher vinylogues (II; R′ = H). It is also used for dimethin*mero*cyanines carrying a chain substituent (II; R′ ≠ H) although the preparation of the intermediate (I; R′ ≠ H) usually involves a number of steps (cf. Brooker, Keyes, Sprague, Van Dyke, Van Lare, Van Zandt, and White, *J. Amer. Chem. Soc.*, 1951, **73**,

5326). In all cases the preparation of (I; $n > 0$) requires, as intermediate, the reactive methyl derivative of the quaternary salt (I; $n = 0$, G = Me) and in certain cases such derivatives are not readily accessible.

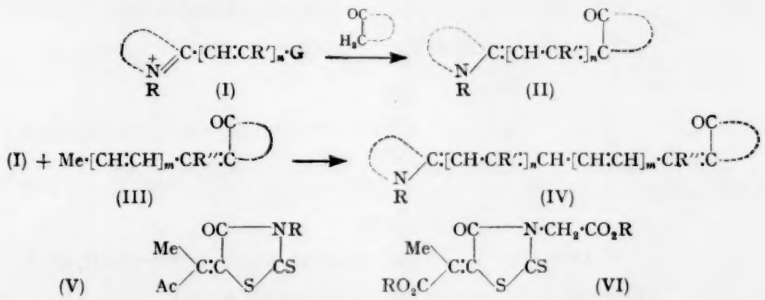
The discovery by Kendall and his co-workers, that the terminal methyl group of alkylidene derivatives (III; R″ = H, alkyl, or aryl) of pyrazolones, rhodanines, or 2-thiohydantoins (with Collins, B.P. 528,803/1939) or of 1′-alkoxyethylidene derivatives (III; $m = 0$, R″ = OEt) of pyrazolones (with Fry and Morgan, B.P. 672,291/1950) still showed the same nucleophilic reactivity associated with the original methylene carbon atom, established a novel method of preparing di- or tetra-methin*mero*cyanines (IV) with or without chain substituents.

Apart from the examples given in the above patents this reaction has not been exploited and the purpose of the present paper is to extend its scope and, in particular, to apply it to the synthesis of complex di- and tetra-methin*mero*cyanines not hitherto accessible.

5-*Alkylidenerhodanines.*—5-Ethylidene- and 5-but-2′-en-1′-ylidene-rhodanine have been prepared by heating rhodanine and paraldehyde or crotonaldehyde in acetic acid (Andreasch, *Monatsh.*, **1918**, **39**, 423; Gränacher, Gerö, Ofner, Kloppenstein, and Schlatter, *Helv. Chim. Acta*, **1923**, **6**, 458). It has now been found that acetaldehyde or crotonaldehyde readily condensed with 3-substituted rhodanines in acetic anhydride–sodium acetate, to give the ethylidene and butenylidene derivatives.

The condensation of acetone and pyrazolones occurs under reflux (Knorr, *loc. cit.*). On the other hand, rhodanine requires as catalyst either sodium acetate in acetic acid (Culvenor, Davies, Maclaren, Nelson, and Savige, *J.*, 1949, 2573) or ammonia and ammonium chloride (Brown, Bradshaw, McCallum, and Potter, *J. Org. Chem.*, 1950, **15**, 174; see also Allan, Maclean, and Newbold, *J.*, 1952, 5053). Cook and Cox (*J.*, 1949, 2343) used pyridine and morpholine for the condensation with 1 : 3-disubstituted 2-thiohydantoin. The 3-substituted rhodanines, it has now been found, condense best with acetone in the presence of zinc chloride.

Zinc chloride is also effective in the condensation of 3-substituted rhodanines with diacetyl, to give the 5-(3-oxobutan-2-ylidene) derivative (V; *i.e.*, III, $m = 0$, R″ = Ac), and with pyruvic acid to give 5-1′-alkoxycarbonylethylidene derivatives (VI), esterification accompanying condensation in alcohol. Both (V) and (VI) are strong photographic desensitizers. This was expected (cf. Kendall, Int. Congr. Photography, Paris, 1935) since both compounds contain the system of two $+M$ atoms connected by a conjugated chain of an even number of carbon atoms. Only one of the two possible geometrical isomers of each of these compounds was isolated and from steric considerations this is assumed to be the one with the configuration shown.



Simple mero*Cyanines and Vinylogues.*—All the above compounds contain a nucleophilic methyl group and can be condensed with suitable intermediates to give vinylogues of *mero*cyanines. The photographic desensitizing properties of (V) and (VI) are considerably enhanced in the dyes derived from them, possibly as a result of the stronger adsorption of the latter on the silver halide grains.

The 1′-alkoxy-, 1′-alkylthio-, and 1′-arylthio-ethylidene derivatives described in the previous paper may also be condensed with 2-alkylthio-derivatives of cyclic ammonium

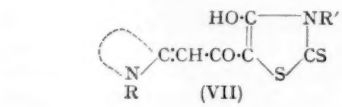
salts (I; $n = 0$, G = SR) (cf. Kendal, Fry, and Morgan, *loc. cit.*), to give dimethin*mero*cyanines containing a chain alkoxy- or alkyl(aryl)thio-group (IV; $n = m = 0$, R″ = RO or RS). Other dyes of the type (IV; $n = m = 0$, R″ = SR) have also been obtained by Edwards and Kendall (U.S.P. 2,531,913) by a different method. One of these dyes, 3-ethoxycarbonylmethyl-5-[1-ethylthio-2-(3-methylthiazolidin-2-ylidene)ethylidene]-2-thiothiazolid-4-one was isolated in three crystalline forms, each of different melting point, but having the same absorption and photographic sensitization characteristics. The form first obtained consisted of well-defined crystals, m. p. 139—143°, which on further recrystallization separated into two forms, m. p. 152—154° and 131° respectively.

In general the replacement of R′ = H by R′ = OEt in (II) results in a hypsochromic absorption shift, whilst replacement by R′ = SR always gives a strong bathochromic shift.

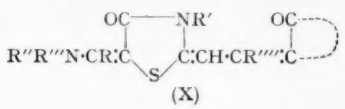
Dimethin*mero*cyanines substituted by alkoxyl in the chain, derived from rhodanines, are rapidly hydrolysed by strong alkali to the alkali-soluble ketones (VII).

Condensation of (III; $m = 0$, R″ = OR or SR) with 2-2′-acetanilidovinyl derivatives (I; $n = 1$, G = NAcPh) proceeds smoothly, to give higher vinylogues of the above dyes (IV; R″ = OR, SR, $m = 0$, $n = 1$).

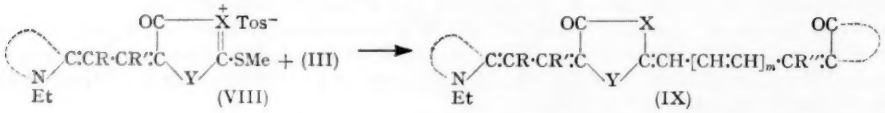
Complex mero*Cyanines*.—The formation of complex *mero*cyanines by reaction of a ketomethylene compound with a quaternized *mero*cyanine (VIII; X ≠ Y = NR or S) derived from a rhodanine or 3-alkyl-2-thiothiazolid-5-one is well known (Kendall, B.P. 487,051; Brooker, in Mees, "The Theory of the Photographic Process," Macmillan, New York, 1942, p. 1038; Knott and Jeffreys, *J.*, 1952, 4762). Such dyes are all characterized by ketonic nuclei attached directly to each other as in simple *mero*cyanines, *i.e.*, :CH·[CH:CH]$_m$·CR″: of (IX) is absent. In order to obtain higher vinylogues (IX; R″ = H) Brooker (personal communication) first converted the SMe group of (VIII) into Me, and brought about the reaction of the product with diphenylformamidine, to give the



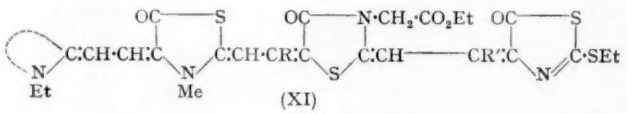
(VII)



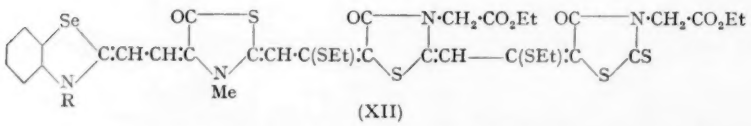
(X)



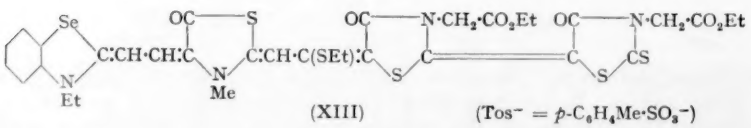
(VIII) (IX)



(XI)



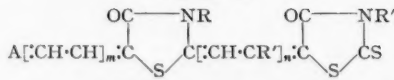
(XII)



(XIII) (Tos⁻ = *p*-C$_6$H$_4$Me·SO$_3$⁻)

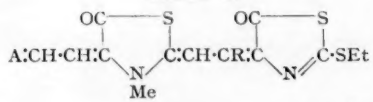
intermediate analogous to (I). Condensation of (VIII) with (III) which proceeds smoothly offers, however, a much more convenient method, in certain cases, of preparing (IX; R″ = H) and allows the ready synthesis of chain-substituted analogues (IX; R″ = Me, OR, SR, Ac, or CO_2R). Such dyes, in which $m = 0$ and R″ = OR or SR, are of particular

TABLE 1.



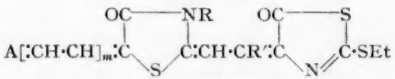
A	R	R′	R″	Yield (%)	Appearance	M. p.	$\lambda_{max.}$ (mμ) (pyridine)	Formula	Found (%) N	Found (%) S	Required (%) N	Required (%) S
3-R-2-[2-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-R′-*ethylidene*]-5-(A-2-*ylidene-ethylidene*)*thiazolid*-4-*one* ($m = n = 1$)												
3-Ethylbenzoxazolin	Et	H	$CH_2{\cdot}CO_2Et$	16·5	Green needles	275°	610	$C_{28}H_{25}O_5N_3S_3$	7·6	17·7	7·75	17·7
,,	,,	OMe	,,	51	,,	244	605	$C_{26}H_{27}O_6N_3S_3$	7·35	—	7·35	—
,,	,,	OEt	,,	41	,,	223	600	$C_{27}H_{29}O_6N_3S_3$	6·8	16·4	7·15	16·35
,,	,,	SEt	,,	65	Green bronze	224	635	$C_{27}H_{29}O_5N_3S_4$	6·7	21·2	6·95	21·2
,,	,,	Ac	,,	50	threads							
3-Ethylbenzothiazolin	Allyl	H	Allyl	37	Green needles	237	622	$C_{27}H_{27}O_6N_3S_3$	7·0	—	6·95	—
,,	,,	OEt	,,	39	Bronze needles	236	616	$C_{28}H_{29}O_6N_3S_4$	7·95	—	8·0	—
3-Ethyl-4 : 5-diphenyl oxazolin	$CH_2{\cdot}CO_2Et$	,,	$CH_2{\cdot}CO_2Et$	38	Green needles	227	620	$C_{27}H_{27}O_6N_3S_4$	7·5	—	7·35	—
3-Ethyl-4 : 5-diphenylthiazolin	,,	,,	,,	37	Bronze-green	151	635	$C_{37}H_{37}O_6N_3S_3$	5·3	12·6	5·6	12·85
3-Ethylnaphtho(1′ : 2′-4 : 5)-thiazolin	Allyl	,,	Allyl	39	Green needles	192	645	$C_{37}H_{37}O_7N_3S_4$	5·5	16·7	5·5	16·8
3-Ethylbenzoselenazolin-	$CH_2{\cdot}CO_2Et$	,,	$CH_2{\cdot}CO_2Et$	37	,,	209	670	$C_{33}H_{33}O_6N_3S_4$	6·3	17·0	6·5	17·15
3-Methylthiazolidin-	,,	,,	,,	33	,,	221	625	$C_{29}H_{31}O_7N_3S_3Se$	5·8	—	5·95	—
1 : 3 : 3-Trimethylindolin	Et	,,	,,	33	Brilliant green	211	590	$C_{24}H_{29}O_7N_3S_4$	6·8	21·2	7·0	21·4
1 : 3-Diethylbenzimidazolin	$CH_2{\cdot}CO_2Et$	,,	,,	28	Green flakes	212	600	$C_{29}H_{33}O_5N_3S_3$	6·7	16·0	7·0	16·0
1-Ethyl-1 : 2-dihydropyridin	,,	,,	,,	62	Brilliant green	212	650	$C_{31}H_{36}O_7N_4S_3$	8·3	14·1	8·35	14·3
1-Ethyl-1 : 4-dihydropyridin-4-	,,	,,	,,	33	Green threads	179	665	$C_{27}H_{31}O_7N_3S_3$	6·85	15·7	6·95	15·85
1-Ethyl-1 : 2-dihydroquinolin	,,	,,	,,	40	Green flakes	213	685	,,	6·8	15·8	6·95	15·85
1-Ethyl-1 : 4-dihydroquinolin-4-	,,	,,	,,	30	,,	216	660	$C_{31}H_{33}O_7N_3S_3$	6·35	14·5	6·4	14·65
	,,	,,	,,		Green-gold needles	210	690	,,	6·5	14·3	,,	,,
3-R-2-[2-(3-*Allyl*-4-*oxo*-2-*thiothiazolid*-5-*ylidene*)*prop*-1-*ylidene*]-5-(A-2-*ylidene-ethylidene*)*thiazolid*-4-*one* ($m = n = 1$; R′ = Me; R″ = allyl)												
3-Ethylbenzoxazolin	R Et			43	Green needles	264	611	$C_{25}H_{25}O_3N_3S_3$	8·3	18·9	8·2	18·8
3-Ethylbenzothiazolin	Allyl			33	,,	266	630	$C_{26}H_{25}O_2N_3S_4$	7·8	—	7·8	—
3-R-2-[4-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)*but*-2-*en*-1-*ylidene*]-5-(A-2-*ylidene-ethylidene*)*thiazolid*-4-*one* ($m = 1$; $n = 2$; R′ = H)												
3-Ethylbenzoxazolin	R Et		R″ Allyl	19	Gold-green needles	282	643	$C_{26}H_{25}O_3N_3S_3$	7·9	18·3	8·05	18·35
,,	,,		$CH_2{\cdot}CO_2Et$	16	Grey	270	635	$C_{27}H_{27}O_5N_3S_3$	7·6	—	7·4	—
3-Ethylbenzothiazolin	Allyl		Allyl	33	Bronze needles	239	658	$C_{27}H_{25}O_2N_3S_4$	7·55	23·2	7·55	23·25
3-R-2-[2-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-R′-*ethylidene*]-5-A-*thiazolid*-4-*one* ($m = 0$; $n = 1$)												
3-Ethylbenzthiazolin-2-ylidene	R Et	R′ OEt	R″ $CH_2{\cdot}CO_2Et$	96	Mauve	250	595	$C_{33}H_{33}O_5N_3S_4$	6·05	18·7	6·3	18·85
Piperid-1′-ylmethylene	$CH_2{\cdot}CO_2Et$	H	,,	33	Rust threads	196	529	$C_{22}H_{27}O_6N_3S_3$	7·7	18·3	8·0	18·3
,,	,,	OMe	,,	36	Red needles	129	528	$C_{23}H_{29}O_7N_3S_3$	7·5	—	7·65	—
Piperid-1′-ylmethylene	,,	SEt	,,	24	Magenta threads	168	561	$C_{24}H_{31}O_6N_3S_4$	7·5	21·7	7·2	21·9
n-Octylaminomethylene	Allyl	OEt	Allyl	29	Green plates	138—140	522	$C_{25}H_{35}O_5N_3S_3$	7·9	—	8·05	—
3-R-2-[2-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)*prop*-2-*ylidene*)-5-A-*thiazolid*-4-*one* ($m = 0$; $n = 1$; R′ = Me)												
n-Octylaminomethylene	R Allyl		R″ Allyl	32·5	Green-red threads	138	540	$C_{24}H_{33}O_2N_3S_3$	8·5	19·3	8·55	19·6
Piperid-1′-ylmethylene	$CH_2{\cdot}CO_2Et$		$CH_2{\cdot}CO_2Et$	31	Pink needles	200	529	$C_{23}H_{24}O_6N_3S_3$	7·75	—	7·85	—

TABLE 2.



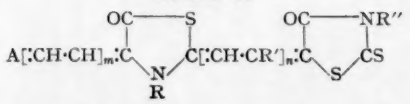
A	R	Yield (%)	Appearance	M. p.	$\lambda_{max.}$ (mμ) (pyridine)	Formula	Found (%) N	Found (%) S	Required (%) N	Required (%) S
2-[2-R-2-(2-*Ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]-4-(A-2-*ylidene-ethylidene*)-3-*methylthiazolid*-5-*one*										
3-Ethylbenzoxazolin	OEt	35	Green needles	229°	640	$C_{24}H_{25}O_4N_3S_3$	7·95	—	8·15	—
,, ...	SEt	34	,,	203	680	$C_{24}H_{25}O_3N_3S_4$	7·65	24·2	7·9	24·1
3-Ethylbenzothiazolin	OEt	19	,,	251	660	$C_{24}H_{25}O_3N_3S_4$	7·75	24·1	7·9	24·1
,, ...	SEt	33	Bronze threads	203	714	$C_{24}H_{25}O_2N_3S_5$	7·8	29·05	7·7	29·3

TABLE 3.



A	R	R′	Yield (%)	Appearance	M. p.	$\lambda_{max.}$ (mμ) (pyridine)	Formula	Found (%) N	Found (%) S	Required (%) N	Required (%) S
3-R-2-[2-R′-2-(2-*Ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]-5-(A-2-*ylidene-ethylidene*)*thiazolid*-4-*one* (m = 1)											
3-Ethylbenzoxazolin	Et	OEt	23	Green needles	209°	588	$C_{25}H_{27}O_4N_3S_3$	7·9	—	7·95	—
,, ...	,,	SEt	53	Brassy needles	194	635	$C_{25}H_{27}O_3N_3S_4$	7·6	23·3	7·7	23·5
3-Ethylbenzothiazolin	,,	OEt	33	Green needles	227	610	$C_{25}H_{27}O_3N_3S_4$	7·55	23·05	7·7	23·5
,, ...	,,	SEt	48	Brown needles	198	650	$C_{25}H_{27}O_2N_3S_5$	7·2	28·65	7·5	28·5
3-Ethyl-4 : 5-diphenylthiazolin	$CH_2{\cdot}CO_2Et$	OEt	18	Coppery needles	240	630	$C_{35}H_{35}O_5N_3S_4$	5·85	18·05	5·95	18·15
,,	...	SEt	34	Bronze needles	205	675	$C_{35}H_{35}O_4N_3S_5$	5·7	22·0	5·85	22·2
3-*Allyl*-2-[2-R′-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]-5-A-*thiazolid*-4-*one* (m = 0)											
Morpholin-3′-ylmethylene	—	OEt	34	Magenta threads	176	518	$C_{20}H_{25}O_4N_3S_3$	8·85	—	9·0	—
,, ...	—	SEt	19	Black flakes	146	567	$C_{20}H_{25}O_3N_3S_4$	8·4	26·3	8·7	26·5

TABLE 4.



A	R′	R″	Yield (%)	Appearance	M. p.	$\lambda_{max.}$ (mμ) (pyridine)	Formula	Found (%) N	Found (%) S	Required (%) N	Required (%) S
2-[2-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-R′-*ethylidene*]-4-(A-2-*ylidene-ethylidene*)-3-R-*thiazolid*-4-*one* ($m = n = 1$; R = Me)											
3-Ethylbenzoxazolin	H	$CH_2{\cdot}CO_2Et$	32	Green needles	303°	644	$C_{24}H_{22}O_5N_2S_3$	7·7	17·9	7·95	18·2
,,	OMe	,,	18	,,	235	643	$C_{25}H_{24}O_6N_2S_3$	7·6	—	7·5	—
,,	OEt	,,	32	Brilliant green	231	650	$C_{26}H_{27}O_6N_3S_3$	7·05	16·5	7·35	16·75
,, *	,,	,,	46	Green needles	241	650	$C_{27}H_{29}O_6N_3S_3$	7·25	—	7·15	—
,,	SEt	,,	34	Green tablets	257	691	$C_{26}H_{27}O_5N_3S_4$	7·05	21·5	7·15	21·75
,, *	,,	,,	55	Gold-green	238	690	$C_{27}H_{29}O_5N_3S_4$	6·75	—	6·95	—
3-Ethylbenzothiazolin	OEt	,,	34	Dark green	241	676	$C_{26}H_{27}O_5N_3S_4$	7·15	21·6	7·15	21·75
,, *	,,	,,	43	Bronze	240	675	$C_{27}H_{29}O_5N_3S_4$	7·2	21·1	6·95	21·2
,,	OMe	,,	31	Green needles	215	676	$C_{25}H_{25}O_5N_3S_4$	7·3	22·3	7·3	22·3
,,	SEt	,,	35	Green–bronze threads	239	718	$C_{26}H_{27}O_4N_3S_5$	6·75	26·3	6·95	26·5
,, *	,,	,,	45	Brassy-green	233	720	$C_{27}H_{29}O_4N_3S_5$	—	25·7	—	25·85
,,	$S{\cdot}CH_2Ph$	,,	32	Green needles	240	718	$C_{31}H_{29}O_4N_3S_5$	6·35	—	6·3	—
3-Ethyl-4 : 5-diphenyloxazolin	H	Allyl	20	Green threads	237	660	$C_{31}H_{27}O_3N_3S_3$	7·0	—	7·2	—
,,	OEt	,,	29	Green needles	255	660	$C_{33}H_{31}O_4N_3S_3$	6·8	—	6·7	—
3-Ethyl-4 : 5-diphenylthiazolin	H	,,	40	,,	279	682	$C_{31}H_{27}O_3N_3S_4$	7·05	21·5	7·0	21·3
,,	OEt	,,	40	,,	252	710	$C_{33}H_{31}O_3N_3S_4$	6·55	19·6	6·5	19·85
,,	SEt	$CH_2{\cdot}CO_2Et$	72	Golden threads	264	752	$C_{34}H_{33}O_4N_3S_5$	—	22·5	—	22·4
3-Ethylbenzoselenazolin	OEt	,,	37	Green needles	244	685	$C_{26}H_{27}O_5N_3S_2Se$	6·65	—	6·6	—
,,	SEt	,,	49	,,	236	726	$C_{26}H_{27}O_4N_3S_3Se$	6·55	—	6·45	—
3-Ethylthiazolidin	OEt	,,	45	,,	197	639	$C_{22}H_{27}O_5N_3S_4$	7·45	—	7·75	—
,,	SEt	,,	51	Green flakes	227	676	$C_{22}H_{27}O_4N_3S_5$	7·3	28·6	7·55	28·7
3-Ethylnaphtho(1′ : 2′-4 : 5)thiazolin	OEt	,,	38	Green needles	260	705	$C_{30}H_{29}O_5N_3S_4$	6·65	19·7	6·6	20·0
2-[2-(3-R″-4-*Oxo*-2-*thiothiazolidin*-5-*ylidene*)*prop*-1-*ylidene*]-4-(A-2-*ylidene-ethylidene*)-3-*methylthiazolid*-5-*one* ($m = n = 1$; R′ = Me)											
	R″										
3-Ethylbenzoxazolin-	$CH_2{\cdot}CO_2Et$		37	Green needles	264	665	$C_{28}H_{23}O_5N_3S_3$	7·6	—	7·75	—
3-Ethyl-4 : 5-diphenyloxazolin	$CH_2{\cdot}CH{:}CH_2$		38	,,	275	671	$C_{32}H_{29}O_3N_3S_3$	7·05	—	7·05	—
3-Ethyl-4 : 5-diphenylthiazolin	,,		54	Green-bronze needles	277	730	$C_{32}H_{29}O_2N_3S_4$	6·95	20·7	6·85	20·8
2-[4-(3-*Ethoxycarbonylmethyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)*but*-2-*en*-1-*ylidene*]-4-(A-2-*ylidene-ethylidene*)-3-*methylthiazolid*-5-*one* ($m = 1$; $n = 2$; R′ = H, R″ = $CH_2{\cdot}CO_2Et$)											
3-Ethylbenzoxazolin			14	Green needles	275	725	$C_{26}H_{25}O_5N_3S_3$	7·55	17·25	7·55	17·3
3-Ethylbenzothiazolin			21	Green-gold	273	758	$C_{26}H_{25}O_4N_3S_4$	7·25	22·4	7·35	22·4
3-Ethyl-4 : 5-diphenyloxazolin			11·5	Bronze flakes	305	755	$C_{34}H_{31}O_5N_3S_3$	6·4	14·3	6·4	14·6
3-Ethyl-4 : 5-diphenylthiazolin			27	Green flakes	298	780	$C_{34}H_{31}O_4N_3S_4$	6·1	19·1	6·25	19·0

* R = Et.

interest because these chain groups considerably increase the solubility of the dyes, which otherwise are difficultly soluble in common organic solvents. As with the simpler dyes, replacement of R'' = H by R'' = SEt in (IX) causes a strong bathochromic shift.

Similarly, quaternized oxamines (see preceding paper) condensed with (III; $m = 0$) to give complex dyes (X). These, like the lower vinylogues (preceding paper) are much lighter in colour than the related complex *mero*cyanines. The details of the complex dyes are given in Tables 1—4.

Even more complex tetranuclear dyes (XI—XIII) have also been synthesized from (IX; R'' = OEt or SEt; $m = 0$), where the end ketonic nucleus is 3-ethoxycarbonylmethylrhodanine, by a repetition of the procedure used in making the trinuclear dyes. Dyes (XI) and (XII) are remarkable in showing a lower m. p. than the parent trinuclear dyes, and are soluble in benzene or acetone. Their main absorption band lies almost completely in the infra-red region, a phenomenon which is believed to be unique amongst non-ionic dyes. The degraded blue colour of their solutions is a result of minor absorption bands which appear to be characteristic of these dyes.

Experimental

Determinations of $\lambda_{max.}$ refer to MeOH solution unless otherwise stated.

3-Ethoxycarbonylmethyl-5-ethylidene-2-thiothiazolid-4-one.—3-Ethoxycarbonylmethylrhodanine (2·2 g.), acetaldehyde (1 c.c.), acetic anhydride (10 c.c.), and anhydrous sodium acetate (1·2 g.) were refluxed for 1 hr. on the steam-bath, with the addition of acetaldehyde (1 c.c.) every 15 min. Acetic acid (5 c.c.) was added and the mixture poured into water, to give a yellow oil which soon solidified. The *product* (2·45 g., 100%) formed slender, pale yellow needles, m. p. 69°, from *iso*propanol (Found: C, 44·3; H, 4·9; S, 25·9. $C_9H_{11}O_3NS_2$ requires C, 44·05; H, 4·5; S, 26·15%).

3-Allyl-5-ethylidene-2-thiothiazolid-4-one.—3-Allylrhodanine (8·65 g.) anhydrous sodium acetate (6·0 g.), acetic anhydride (50 c.c.), and acetaldehyde (10 c.c.) were heated for 1 hr. in an autoclave in a steam-bath. The mixture was decomposed with dilute acetic acid, and the oil taken up in ether and distilled. The *product* (6·45 g., 65%) had b. p. 119—123°/3 mm., and formed yellow needles, m. p. 37°, from *iso*propanol (Found: S, 32·25. $C_8H_9ONS_2$ requires S, 32·2%).

5-But-2'-en-1'-ylidene-3-ethoxycarbonylmethyl-2-thiothiazolid-4-one.—3-Ethoxycarbonylmethylrhodanine (11·0 g.), crotonaldehyde (9·0 c.c.), acetic anhydride (75 c.c.), and anhydrous sodium acetate (6·0 g.) were refluxed together for 10 min. Most of the solvent was removed under reduced pressure, and the residue was shaken with water (100 c.c.). The *product* soon solidified, forming orange needles, m. p. 104° (6·0 g., 44·5%), from *iso*propanol (Found: C, 48·85; H, 5·05; S, 23·4. $C_{11}H_{13}O_3NS_2$ requires C, 48·7; H, 4·8; S, 23·6%).

3-Allyl-5-but-2'-en-1'-ylidene-2-thiothiazolid-4-one was obtained similarly in 51·5% yield as orange-yellow needles, m. p. 92°, from *iso*propanol. The solutions in the latter solvent should be chilled rapidly to prevent a slight stickiness (Found: C, 53·1; H, 5·0; S, 28·05. $C_{10}H_{11}ONS_2$ requires C, 53·3; H, 4·9; S, 28·45%).

5-But-2'-en-1'-ylidene-3-ethyl-2-thiothiazolid-4-one formed brown flakes, m. p. 87—88°, from *iso*propanol (63% yield) (Found: C, 51·15; H, 5·5; S, 29·9. $C_9H_{11}ONS_2$ requires C, 51·25; H, 5·2; S, 30·3%).

3-Ethoxycarbonylmethyl-5-prop-2'-ylidene-2-thiothiazolid-4-one.—3-Ethoxycarbonylmethylrhodanine (22·0 g.), powdered anhydrous zinc chloride (30·0 g.), and dry acetone (250 c.c.) were heated for 4 hr. in an autoclave in a steam-bath. Water (1 l.) was added, to precipitate the *product* which solidified. It (16·6 g., 64%) formed soft, pale yellow needles, m. p. 75°, from *iso*propanol (Found: C, 46·1; H, 5·1; N, 5·35; S, 24·5. $C_{10}H_{13}O_3NS_2$ requires C, 46·3; H, 5·0; N, 5·4; S, 24·7%).

3-Carboxymethyl-5-prop-2'-ylidene-2-thiothiazolid-4-one was obtained similarly in 26% yield as pale yellow flakes, m. p. 162—168° from aqueous ethanol (Found: C, 41·6; H, 4·1; S, 27·5. $C_8H_9O_3NS_2$ requires C, 41·65; H, 3·9; S, 27·7%).

3-Allyl-5-prop-2'-ylidene-2-thiothiazolid-4-one.—3-Allylrhodanine (17·3 g.), zinc chloride (27 g.), and acetone (250 c.c.) were heated for 8 hr. in an autoclave in a steam-bath. The solid (18·5 g., 87%) obtained on precipitation with water formed pale, lemon-yellow needles, m. p. 53°, from *iso*propanol (Found: C, 50·3; H, 5·15; S, 30·1. $C_9H_{11}ONS_2$ requires C, 50·7; H, 5·15; S, 30·05%).

3-Ethoxycarbonylmethyl-5-(3-oxobut-2-ylidene)-2-thiothiazolid-4-one (V; R = $CH_2{\cdot}CO_2Et$).—

3-Ethoxycarbonylmethylrhodanine (4·4 g.), diacetyl (1·8 c.c.), powdered zinc chloride (5·4 g.), and dioxan (10 c.c.) were heated for 5 hr. on a steam-bath. Addition of water (25 c.c.) to the deep yellow solution precipitated an oil which partly crystallized. The aqueous layer was decanted and the residue triturated with ethanol (15 c.c.). The solid (1·8 g., 31·5%), washed with ethanol formed long yellow needles, m. p. 111°, from ethanol (Found: C, 46·2; H, 4·3; N, 4·9; S, 21·9. $C_{11}H_{13}O_4NS_2$ requires C, 46·0; H, 4·55; N, 4·9; S, 22·3%).

3-*Carboxymethyl*-5-(3-*oxobut*-2-*ylidene*)-2-*thiothiazolid*-4-*one* (V; R = $CH_2{\cdot}CO_2H$).—3-Carboxymethylrhodanine (7·65 g.), diacetyl (3·6 c.c.), zinc chloride (10·8 g.), and dioxan (20 c.c.) were heated for 5 hr. on a steam-bath. The addition of water precipitated yellow grains. The *product* (7·15 g., 77·5%) formed fine, yellow needles, m. p. 207°, from methanol (Found: C, 41·9; H, 3·5; S, 24·6. $C_9H_9O_4NS_2$ requires C, 41·7; H, 3·5; S, 24·7%).

When the reaction was carried out in *n*-butanol for 20 hr., the n-*butyl ester* (7·7 g.) was obtained and formed long yellow needles, m. p. 58—59°, from methanol (Found: C, 49·5; H, 5·4; N, 4·35; S, 20·4. $C_{13}H_{17}O_4NS_2$ requires C, 49·5; H, 5·4; N, 4·45; S, 20·35%).

5-1′-*Methoxycarbonylethylidene*-3-*methoxycarbonylmethyl*-2-*thiothiazolid*-4-*one* (VI; R = Me).—3-Carboxymethylrhodanine (9·5 g.), pyruvic acid (5 c.c.), methanol (35 c.c.), and zinc chloride (13·5 g.) were refluxed together for 17 hr. and treated with water. The solid (7·4 g., 59%) obtained on chilling formed flat, yellow needles, m. p. 87—88°, from *iso*propanol (Found: C, 42·1; H, 3·9; S, 21·9. $C_{10}H_{11}O_5NS_2$ requires C, 41·8; H, 3·8; S, 22·15%). Employing other alcohols as solvents gave the *diethyl*, yellow needles, m. p. 68° (from *iso*propanol; 49% yield) (Found: C, 45·2; H, 4·5; S, 20·15. $C_{12}H_{15}O_5NS_2$ requires C, 45·4; H, 4·7; S, 20·2%), and the *di*-n-*butyl ester* (52%), soft, yellow needles, m. p. 52° (from methanol) (Found: C, 51·3; H, 5·9; N, 3·9; S, 17·05. $C_{16}H_{23}O_5NS_2$ requires C, 51·5; H, 6·15; N, 3·75; S, 17·15%).

3-*Allyl*-5-[4-(3-*ethylbenzothiazolin*-2-*ylidene*)*but*-2-*en*-1-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; R″ = H, *n* = 0, *m* = 1).—2-Ethylthiobenzothiazole ethotoluene-*p*-sulphonate (2·0 g.), 3-allyl-5-but-2′-en-1′-ylidenerhodanine (1·2 g.), pyridine (10 c.c.), and triethylamine (0·8 c.c.) were heated on the steam-bath for 30 min. Ethanol (20 c.c.) was added and the whole was chilled overnight. The *dye* (1·1 g., 57%) which separated formed blue needles, m. p. 220°, from benzene (Found: N, 7·2; S, 24·75. $C_{19}H_{18}ON_2S_3$ requires N, 7·25; S, 24·9%), $\lambda_{max.}$ 605 mμ.

3-*Allyl*-5-[6-(3-*ethylbenzothiazolin*-2-*ylidene*)*hexa*-2 : 4-*dien*-1-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; R′ = R″ = H, *n* = *m* = 1).—2-2′-Acetanilidovinylbenzothiazole ethiodide (2·25 g.), 3-allyl-5-but-2′-en-1′-ylidenerhodanine (1·15 g.), pyridine (10 c.c.), and triethylamine (0·8 c.c.) were heated for 30 min. on a steam-bath and then diluted with ethanol (20 c.c.). The *dye* separated rapidly, forming brilliant, green needles, m. p. 212° (1·0 g., 49·5%), from benzene (Found: N, 6·65; S, 23·25. $C_{21}H_{20}ON_2S_3$ requires N, 6·8; S, 23·3%), $\lambda_{max.}$ 630 mμ.

3-*Allyl*-5-{1-[3-*ethylnaphtho*(1′ : 2′-4 : 5)*thiazolin*-2-*ylidene*]*pent*-2-*en*-4-*ylidene*}-2-*thiothiazolid*-4-*one* (IV; *n* = 0, *m* = 1, R″ = Me).—2-2′-Acetanilidovinylnaphtho(1′ : 2′-4 : 5)thiazole ethiodide (2·5 g.), 3-allyl-5-prop-2′-ylidenerhodanine (1·1 g.), pyridine (10 c.c.), and triethylamine (0·8 c.c.) were heated on a steam-bath for 30 min. Ethanol (20 c.c.) was added to precipitate 1·4 g. (62·0%) of *dye*. It formed blue needles, m. p. 245°, from pyridine–ethanol (Found: N, 6·4; S, 21·2. $C_{24}H_{22}ON_2S_3$ requires N, 6·2; S, 21·35%), $\lambda_{max.}$ 610 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)-5-*oxohex*-2-*en*-4-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; *n* = 0, *m* = 1, R″ = Ac).—2-2′-Acetanilidovinylbenzothiazole ethotoluene-*p*-sulphonate (2·25 g.), 5-(3-oxobutan-2-ylidene)-3-ethoxycarbonylmethylrhodanine (1·45 g.), ethanol (10 c.c.), and triethylamine were refluxed together for 15 min. The dye was precipitated as a tar, on chilling of the mixture. Ethanol (10 c.c.) was added and the mixture was boiled until crystallization set in. The *dye* (1·0 g., 42%) formed a dark blue powder, m. p. 156°, from ethanol (Found: C, 55·6; H, 4·6; N, 5·65. $C_{22}H_{24}O_4N_2S_3$ requires C, 55·75; H, 4·65; N, 5·9%), $\lambda_{max.}$ 653 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)-3-*oxobut*-2-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; *m* = *n* = 0, R″ = Ac).—2-Ethylthiobenzothiazole ethotoluene-*p*-sulphonate (2·0 g.), 3-ethoxycarbonylmethyl-5-(3-oxobutan-2-ylidene)rhodanine (1·4 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 5 min. The *dye* separated from the hot solution. It (1·4 g., 62·5%) formed rosettes of blue needles, m. p. 195°, from benzene (Found: N, 6·2; S, 21·35. $C_{20}H_{20}O_4N_2S_3$ requires N, 6·25; S, 21·4%), $\lambda_{max.}$ 520 mμ.

3-*Methoxycarbonylmethyl*-5-[1-*methoxycarbonyl*-2-(3-*methylthiazolidin*-2-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one* (IV; *m* = *n* = 0, R″ = CO_2Me).—2-Methylthiothiazoline methotoluene-*p*-sulphonate (1·6 g.), 3-methoxycarbonyl-5-1′-methoxycarbonylethylidenerhodanine (1·45 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 10 min. The *dye* (1·0 g., 51·5%) separated as an oil and then crystallized slowly when chilled. It formed red

needles or steel-blue prisms, m. p. 178°, from benzene–ethanol (Found: N, 7·05; S, 24·7. $C_{14}H_{16}O_5N_2S_3$ requires N, 7·2; S, 24·75%), $\lambda_{max.}$ 462 mμ.

4-[1-*Ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]-2-*phenyloxazol*-5-*one* (IV; $n = m = 0$, R″ = OEt).—2-Ethylthiobenzothiazole ethotoluene-*p*-sulphonate (2·0 g.), 4-1′-ethoxyethylidene-2-phenyloxazol-5-one (1·15 g.), *n*-propanol (5 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 10 min., then chilled, and the containing vessel was scratched. The *dye* (0·8 g., 50%) formed orange threads, m. p. 198°, from ethanol (Found: C, 66·95; H, 5·05; N, 7·3; S, 8·3. $C_{22}H_{20}O_3N_2S$ requires C, 67·3; H, 5·1; N, 7·15; S, 8·15%), $\lambda_{max.}$ 480 mμ.

4-[1-*Ethoxy*-2-(1-*ethyl*-1 : 2-*dihydroquinolin*-2-*ylidene*)*ethylidene*]-2-*ethylthiothiazol*-5-*one*.—4-1′-Ethoxyethylidene-2-ethylthiothiazol-5-one (1·2 g.), 2-ethylthioquinoline ethotoluene-*p*-sulphonate (1·95 g.), pyridine (10 c.c.), and triethylamine (0·8 c.c.) were heated together for 15 min. on the steam-bath. Ethanol (20 c.c.) was added and the solution was chilled. The *dye* (1·05 g., 54·5%), after being washed with ethanol, formed golden-green crystals, m. p. 176°, from methanol (Found: C, 62·55; H, 5·8; N, 6·95; S, 16·4. $C_{20}H_{22}O_2N_2S_2$ requires C, 62·2; H, 5·7; N, 7·25; S, 16·6%). λ_{max} 545 mμ.

The following dyes are a selection of those obtained similarly.

2-[1-*Ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]*indane*-1 : 3-*dione* formed red needles (74% yield), m. p. 195—196°, from ethanol (Found: C, 69·8; H, 4·95. $C_{22}H_{19}O_3NS$ requires C, 70·0; H, 5·05%). $\lambda_{max.}$ 470 mμ.

4-[1-*Ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]-3-*phenylisooxazol*-5-*one* formed pink flakes with a blue reflex (47% yield), m. p. 185°, from ethanol (Found: N, 7·45; S, 8·2. $C_{22}H_{20}O_3N_2S$ requires N, 7·15; S, 8·15%), $\lambda_{max.}$ 448 mμ.

4-[1-*Ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]-3-*methyl*-1-*phenylpyrazol*-5-*one* was obtained in 74% yield as soft rosettes of orange-red needles, m. p. 172°, from ethanol (Found: N, 10·4. $C_{23}H_{22}O_2N_3S$ requires N, 10·35%), $\lambda_{max.}$ 548 mμ.

3-*Ethoxycarbonyl*-5-[1-*ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one*, obtained in 52% yield, formed rosettes of magenta needles, m. p. 127°, from benzene–light petroleum (b. p. 60—80°) (Found: S, 21·1. $C_{20}H_{22}O_4N_2S_3$ requires S, 21·35%), $\lambda_{max.}$ 516 mμ.

4-[1-*Ethoxy*-4-(3-*ethylbenzoxazolin*-2-*ylidene*)*but*-2-*en*-1-*ylidene*]-2-*phenyloxazol*-5-*one* (IV; $n = 0$, $m = 1$, R″ = OEt).—2-2′-Acetanilidovinylbenzoxazole ethiodide (2·2 g.), 4-1′-ethoxyethylidene-2-phenyloxazol-5-one (1·2 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 30 min. The whole solidified when chilled. The *dye* (1·2 g., 85%) formed magenta threads, m. p. 191°, from benzene–ethanol (Found: C, 71·55; H, 5·6; N, 7·1. $C_{24}H_{22}O_4N_2$ requires C, 71·7; H, 5·45; N, 6·95%), $\lambda_{max.}$ 545 mμ.

2-*Benzylthio*-4-[1-*ethoxy*-4-(3-*ethylbenzoxazolin*-2-*ylidene*)*but*-2-*en*-1-*ylidene*]*thiazol*-5-*one* was obtained in 35% yield as blue needles, m. p. 122°, from ethanol (Found: C, 64·5; H, 5·1; N, 6·25; S, 13·9. $C_{25}H_{24}O_3N_2S_2$ requires C, 64·7; H, 5·2; N, 6·05; S, 13·8%), $\lambda_{max.}$ 570 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-*ethoxy*-4-(3-*ethylbenzothiazolin*-2-*ylidene*)*but*-2-*en*-1-*ylidene*]-2-*thiothiazolid*-4-*one*, obtained in 88% yield, formed soft, deep blue needles, m. p. 171°, from benzene–light petroleum (b. p. 60—80°) (Found: N, 5·7; S, 20·1. $C_{22}H_{24}O_4N_2S_3$ requires N, 5·9; S, 20·2%), $\lambda_{max.}$ 610 mμ.

3-*Ethoxycarbonylmethyl*-5-{4-[3-*ethylnaphtho*(1′ : 2′-4 : 5)*thiazolin*-2-*ylidene*]-1-*methoxybut*-2-*en*-1-*ylidene*}-2-*thiothiazolid*-4-*one* (IV; $n = 0$, $m = 1$, R″ = OMe) was obtained in 43% yield as green crystals, m. p. 184°, from benzene–ethanol (Found: N, 5·45; S, 18·7. $C_{25}H_{24}O_4N_2S_3$ requires N, 5·45; S, 18·75%), $\lambda_{max.}$ 642 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-5-[1-*ethoxy*-6-(3-*ethylbenzothiazolin*-2-*ylidene*)*hexa*-2 : 4-*dien*-1-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; $n = m = 1$, R′ = H, R″ = OEt).—2-4′-Acetanilidobuta-2 : 4-dienylbenzothiazole ethiodide (2·4 g.), 3-ethoxycarbonylmethyl-5-1′-ethoxyethylidenerhodanine (1·5 g.), ethanol (20 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 2 min. The mixture was chilled to give a tar. The liquor was decanted, and the tar was washed with ethanol and was then refluxed with ethanol (60 c.c.) until crystallization set in. The dye (1·1 g., 44%) was dissolved in benzene (25 c.c.) and filtered and an equal volume of ethanol was added. The whole was concentrated to 20 c.c. and chilled. The dye crystallized and the process was repeated. The *dye* formed small, bright green crystals, m. p. 187° (Found: C, 57·7; H, 5·25; N, 5·45. $C_{24}H_{26}O_4N_2S_3$ requires C, 57·4; H, 5·2; N, 5·55%), $\lambda_{max.}$ 620 mμ.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylbenzothiazolin*-2-*ylidene*)-1-*ethylthioethylidene*]-2-*thiothiazolid*-4-*one* (IV; $n = m = 0$, R″ = SEt).—2-Ethylthiobenzothiazole ethotoluene-*p*-sulphonate (1·3 g.), 3-ethoxycarbonylmethyl-5-1′-ethylthioethylidenerhodanine (1·0 g.), ethanol (10 c.c.), and triethylamine (0·5 c.c.) were refluxed together for 5 min. The dye (0·9 g., 58%) crystallized when the solution was chilled, and was obtained as flat, green needles, m. p. 157°, from ethanol

(Found: C, 51·7; H, 5·05; N, 6·25; S, 27·4. $C_{20}H_{22}O_3N_2S_4$ requires C, 51·5; H, 4·7; N, 6·0; S, 27·45%), $\lambda_{max.}$ 561 mμ.

3-*Ethoxycarbonylmethyl*-5-[1-*ethylthio*-2-(3-*methylthiazolidin*-2-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one*.—2-Methylthiothiazoline methotoluene-*p*-sulphonate (1·6 g.), 3-ethoxycarbonylmethyl-5-1′-ethylthioethylidenerhodanine (1·5 g.), pyridine (10 c.c.), and triethylamine (0·8 c.c.) were heated together on the steam-bath for 15 min. and diluted with water (25 c.c.). The *dye* was precipitated as an oil which crystallized rapidly. It (1·3 g., 64·5%) formed flat violet needles, m. p. 139—143°, after two crystallizations from ethanol (Found: C, 44·3; H, 4·75; N, 7·1; S, 31·55. $C_{18}H_{20}O_3N_2S_4$ requires C, 44·5; H, 4·95; N, 6·95; S, 31·7%), $\lambda_{max.}$ 515 mμ.

A third crystallization from a more dilute alcoholic solution caused glossy, red flakes (0·9 g.; m. p. 147—149°) to separate, which had m. p. 152—154° after two more crystallizations from alcohol (Found: C, 44·75; H, 5·05; N, 7·25; S, 31·95%), $\lambda_{max.}$ 515 mμ.

The filtrate from the first crystallization gave, on concentration, soft red needles (0·15 g.), m. p. 131°, which on recrystallization from ethanol formed flat red needles, m. p. 131° (Found: C, 45·0; H, 5·3; N, 7·25; S, 32·0%), $\lambda_{max.}$ 515 mμ.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylbenzothiazolin*-2-*ylidene*)-1-p-*tolylthioethylidene*]-2-*thiothiazolid*-4-*one* (IV; $n = m = 0$, R″ = *p*-$C_6H_4Me{\cdot}S{\cdot}$), obtained similarly in 34% yield, formed flat, brassy needles, m. p. 237—239°, from benzene–ethanol (Found: N, 5·25; S, 24·5. $C_{25}H_{24}O_3N_2S_4$ requires N, 5·3; S, 24·25%), $\lambda_{max.}$ 566 mμ.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylbenzothiazolin*-2-*ylidene*)-1-n-*octylthioethylidene*]-2-*thiothiazolid*-4-*one* (IV; $n = m = 0$, R″ = *n*-$C_8H_{17}{\cdot}S{\cdot}$) obtained in 41% yield formed soft, dark green flakes, m. p. 103°, from ethanol (Found: N, 4·95; S, 23·3. $C_{26}H_{34}O_3N_2S_4$ requires N, 5·1; S, 23·3%), $\lambda_{max.}$ 570 mμ.

4-[2-(3-*Ethylbenzothiazolin*-2-*ylidene*)-1-*ethylthioethylidene*]-2-*ethylthiothiazol*-5-*one*.—2-Ethylthiobenzothiazole ethotoluene-*p*-sulphonate (2·0 g.), 2-ethylthio-4-1′-ethylthioethylidenethiazol-5-one (1·1 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.) were refluxed together for 5 min. The *dye* (1·1 g., 54%) which separated on chilling formed large, golden-green aggregates, m. p. 113°, from ethanol (Found: C, 52·75; H, 4·6; N, 7·0; S, 31·3. $C_{18}H_{20}ON_2S_4$ requires C, 52·95; H, 4·9; N, 6·85; S, 31·4%), $\lambda_{max.}$ 557 mμ.

3-*Ethoxycarbonylmethyl*-5-[4-(3-*ethylbenzoxazolin*-2-*ylidene*)-1-*ethylthiobut*-2-*en*-1-*ylidene*]-2-*thiothiazolid*-4-*one* (IV; $n = 0$, $m = 1$, R″ = EtS).—2-2′-Acetanilidovinylbenzoxazole ethiodide (1·45 g.), 3-ethoxycarbonylmethyl-5-1′-ethylthioethylidenerhodanine (1·0 g.), ethanol (10 c.c.), and triethylamine (0·5 c.c.) were refluxed for 5 min. The dye (0·7 g., 44%) which separated on chilling formed blue-green threads, m. p. 172°, from ethanol (Found: C, 55·6; H, 5·05; N, 5·8; S, 19·9. $C_{22}H_{24}O_4N_2S_3$ requires C, 55·5; H, 5·05; N, 5·9; S, 20·2%), $\lambda_{max.}$ 608 mμ.

3-*Ethoxycarbonylmethyl*-5-[4-(3-*ethylbenzothiazolin*-2-*ylidene*]-1-*ethylthiobut*-2-*en*-1-*ylidene*]-2-*thiothiazolid*-4-*one* was obtained in 69% yield and formed flat, blue-green needles, m. p. 174°, from benzene–light petroleum (b. p. 60—80°) (Found: N, 5·85; S, 25·85. $C_{22}H_{24}O_3N_2S_4$ requires N, 5·7; S, 26·0%), $\lambda_{max.}$ 643 mμ.

4-[4-(3-*Ethylbenzothiazolin*-2-*ylidene*)-1-*ethylthiobut*-2-*en*-1-*ylidene*]-2-*ethylthiothiazol*-5-*one* was obtained in 39% yield as flat golden-green needles, m. p. 162°, from benzene–ethanol (Found: S, 30·75. $C_{20}H_{22}ON_2S_4$ requires S, 30·95%), $\lambda_{max.}$ 638 mμ.

Hydrolysis of (IV; $n = m = 0$, R″ = OEt).—3-*Carboxymethyl*-5-(3-*ethylbenzothiazolin*-2-*ylidene*)*acetyl*-4-*hydroxy*-2-*thiothiazoline* (VII). 3-Ethoxycarbonylmethyl-5-[1-ethoxy-2-(3-ethylbenzothiazolin-2-ylidene)ethylidene]-2-thiothiazolid-4-one (0·9 g.), ethanol (20 c.c.), and a solution of potassium hydroxide (0·45 g.) in water (10 c.c.) were refluxed together on a steam-bath for 75 min. The orange solution was acidified to give an orange solid *dye* (0·6 g., 76%). It formed fine, rust red needles, m. p. 222°, from ethanol. It gave a yellow solution in aqueous sodium carbonate (Found: C, 48·5; H, 3·7; N, 6·8; S, 24·55. $C_{16}H_{14}O_4N_2S_3$ requires C, 48·75; H, 3·55; N, 7·1; S, 24·4%), $\lambda_{max.}$ 440 mμ.

3-*Carboxymethyl*-5-(1-*ethyl*-1 : 2-*dihydroquinolin*-2-*ylidene*)*acetyl*-4-*hydroxy*-2-*thiothiazoline* was obtained similarly in 51% yield as violet needles, m. p. 237°, $\lambda_{max.}$ 488 mμ in methanolic triethylamine, by dissolving the dye in alcoholic triethylamine and acidifying the solution with acetic acid (Found: N, 7·25; S, 16·3. $C_{18}H_{16}O_4N_2S_2$ requires N, 7·2; S, 16·5%).

3-*Allyl*-5-(3-*ethylbenzothiazolin*-2-*ylidene*)*acetyl*-4-*hydroxy*-2-*thiothiazoline* was obtained in 64% yield as pink needles, m. p. 199°, from ethanol (Found: C, 54·15; H, 4·55; S, 25·5. $C_{17}H_{16}O_2N_2S_3$ requires C, 54·25; H, 4·25; S, 25·5%, $\lambda_{max.}$ 442 mμ in ethanolic triethylamine.

Complex mero*Cyanines*.—The general procedure for these dyes (IX—XIII) consisted of fusing (IV) (0·01 mol.) with methyl toluene-*p*-sulphonate (0·01—0·015 mol.) at 120—140° for 30—120 min., adding (III) (0·01 mol.), pyridine (20 c.c.), and triethylamine (0·011 mol.) to the

homogeneous melt or solid and heating the whole on the steam-bath for 10 min. The addition of ethanol (50 c.c.) then usually caused the dye to crystallize. It was collected, washed with ethanol, and recrystallized from benzene, or was dissolved in hot pyridine and treated with 2—3 times the volume of hot ethanol. In general 2—3 recrystallizations were necessary to obtain a pure specimen.

3-*Allyl*-2-[2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)*prop*-1-*ylidene*]-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)*prop*-2-*ylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = H, R′ = R″ = Me, Y = S, X = N·C_5H_5) was obtained in 19% yield and formed soft, dark green needles, m. p. 276°, from pyridine–ethanol (Found: N, 7·45; S, 23·2. $C_{27}H_{27}O_2N_3S_4$ requires N, 7·6; S, 23·5%), $\lambda_{max.}$ 648 mμ in pyridine.

3-*Allyl*-2-[2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-*ethoxyethylidene*]-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)*but*-2-*ylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = H, R′ = Et, R″ = OEt, Y = S, X = N·C_5H_5) was obtained in 45% yield and formed soft, green needles, m. p. 209°, from pyridine–ethanol (Found: N, 6·9; S, 21·3. $C_{29}H_{31}O_3N_3S_4$ requires N, 7·05; S, 21·45%), $\lambda_{max.}$ 654 mμ in pyridine.

3-*Allyl*-2-[2-(3-*allyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-*ethoxyethylidene*]-5-[1-*ethoxy*-2-(3-*ethylbenzothiazolin*-2-*ylidene*)*ethylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = H, R′ = R″ = OEt, Y = S, X = N·C_5H_5) was obtained in 12% yield as soft, green needles, m. p. 200°, from benzene–ethanol (Found: N, 6·85; S, 20·9. $C_{29}H_{31}O_4N_3S_4$ requires N, 6·85; S, 20·9%), $\lambda_{max.}$ 645 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-2-[2-(3-*ethoxycarbonylmethyl*-4-*oxo*-2-*thiothiazolidin*-5-*ylidene*)-2-*ethoxyethylidene*]-5-[2-(3-*methylthiazolidin*-2-*ylidene*)*prop*-1-*ylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = Me, R′ = H, R″ = OEt, X = N·CH_2·CO_2Et, Y = S). 3-Ethoxycarbonylmethyl-5-[2-(3-methylthiazolidin-2-ylidene)prop-1-ylidene]-2-thiothiazolid-4-one (1·8 g.) and methyl toluene-*p*-sulphonate (1·0 g.) were fused at 130° for 1 hr. To the viscous melt was added 3-ethoxycarbonylmethyl-5-1′-ethoxyethylidenerhodanine (1·45 g.), ethanol (10 c.c.), and triethylamine (0·8 c.c.), and the whole was refluxed for 10 min. on a steam-bath. The crystals (0·9 g., 30%) collected after chilling formed brilliant green crystals, m. p. 194—195°, from benzene–ethanol (Found: N, 6·5; S, 20·8. $C_{25}H_{31}O_7N_3S_4$ requires N, 6·85; S, 20·9%), $\lambda_{max.}$ 605 mμ in pyridine.

3-*Allyl*-5-[1-(3-*ethylbenzothiazolin*-2-*ylidene*)*but*-2-*ylidene*]-2-[2-*ethylthio*-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = H, R′ = Et, R″ = SEt, X = N·C_5H_5, Y = S) was obtained in 50% yield as black needles (gold reflex), m. p. 147°, from benzene–ethanol (Found: N, 6·95; S, 26·4. $C_{28}H_{31}O_2N_3S_5$ requires N, 7·0; S, 26·6%), $\lambda_{max.}$ 684 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-5-[2-(3-*ethylbenzothiazolin*-2-*ylidene*)-1-*ethylthioethylidene*]-2-[2-*ethylthio*-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]*thiazolid*-4-*one* (IX; $m = 0$, R = H, R′ = R″ = SEt, X = N·CH_2·CO_2Et, Y = S), obtained in 29% yield, formed brassy needles, m. p. 186°, from benzene–ethanol (Found: N, 6·5; S, 28·15. $C_{29}H_{33}O_4N_3S_6$ requires N, 6·2; S, 28·3%), $\lambda_{max.}$ 684 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-2-[2-*ethoxy*-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]-5-{1-*ethoxy*-2-[4-(3-*ethyl*-4 : 5-*diphenylthiazolin*-2-*ylidene*-*ethylidene*)-5-*oxo*-3-*methylthiazolidin*-2-*ylidene*]*ethylidene*}*thiazolid*-4-*one* (XI; R = R′ = OEt). 2-[2-(3-Ethoxycarbonylmethyl-4-oxo-2-thiothiazolidin-5-ylidene)-2-ethoxyethylidene]-4-(3-ethyl-4 : 5-diphenylthiazolin-2-ylidene-ethylidene)-3-methylthiazolid-5-one (1·05 g.) and methyl toluene-*p*-sulphonate (0·5 g.) were fused at 130° in an oil-bath for ½ hr. The melt had then solidified. The cake was broken up, 4-1′-ethoxyethylidene-2-ethylthiothiazol-5-one (0·4 g.), ethanol (20 c.c.), and triethylamine (0·25 c.c.) were added and the whole was refluxed for 5 min. The *dye* separated as an oil from the cooled solution, then crystallized. It (0·75 g., 55·5%) was recrystallized from pyridine–ethanol (green needles, m. p. 244°), then twice from benzene–ethanol, and formed coppery red flakes, m. p. 247° (Found: C, 57·95; H, 4·8; N, 6·3; S, 17·95. $C_{43}H_{44}O_7N_4S_5$ requires C, 58·1; H, 5·0; N, 6·3; S, 18·05%), $\lambda_{max.}$ 772 mμ in pyridine.

3-*Ethoxycarbonylmethyl*-5-{2-[4-(3-*ethyl*-4 : 5-*diphenylthiazolin*-2-*ylidene*-*ethylidene*)-5-*oxo*-3-*methylthiazolidin*-2-*ylidene*]-1-*ethylthioethylidene*}-2-[2-*ethylthio*-2-(2-*ethylthio*-5-*oxothiazolin*-4-*ylidene*)*ethylidene*]*thiazolid*-4-*one* (XI; R = R′ = SEt). 2-[2-(3-Ethoxycarbonylmethyl-4-oxo-2-thiothiazolidin-5-ylidene)-2-ethylthioethylidene]-4-(3-ethyl-4 : 5-diphenylthiazolin-2-ylidene)-3-methylthiazolid-5-one (1·4 g.) and methyl toluene-*p*-sulphonate (0·5 g.) were fused at 130° in an oil-bath for 1 hr. 2-Ethylthio-4-1′-ethylthioethylidenethiazol-5-one (0·6 g.), pyridine (15 c.c.), and triethylamine (0·4 c.c.) were added and the whole was heated for 5 min. on a steam-bath. Ethanol (20 c.c.) was added and heating continued for a further 10 min. After the addition of a

similar quantity of ethanol the solution was chilled. The *dye* (1·3 g., 71·5%) which separated was washed with ethanol and acetone and obtained as soft bronze needles, m. p. 258°, after two recrystallizations from benzene (Found : C, 56·15; H, 4·8; N, 6·0; S, 24·2. $C_{43}H_{44}O_5N_4S_7$ requires C, 56·0; H, 4·8; N, 6·1; S, 24·4%), $\lambda_{max.}$ 865 mμ in pyridine.

3-Ethoxycarbonylmethyl-5-{2-[4-(3-ethylbenzoselenazolin-2-ylidene-ethylidene)-5-oxo-3-methylthiazolidin-2-ylidene]-1-ethylthioethylidene}-2-[2-ethylthio-2-(2-ethylthio-5-oxothiazolin-4-ylidene)-ethylidene]thiazolid-4-one (XI; R = R′ = SEt) was obtained similarly in 62% yield and formed dark golden threads, m. p. 220°, after three recrystallizations from benzene (Found : C, 48·45; H, 4·5; N, 6·85. $C_{35}H_{38}O_5N_4S_6Se$ requires C, 48·6; H, 4·4; N, 6·45%), $\lambda_{max.}$ 822 mμ in pyridine.

3-Ethoxycarbonylmethyl-2-(3-ethoxycarbonylmethyl-4-oxo-2-thiothiazolidin-5-ylidene)-5-{2-[4-(3-ethylbenzoselenazolin-2-ylidene-ethylidene)-5-oxo-3-methylthiazolidin-2-ylidene]-1-ethylthioethylidene}thiazolid-4-one (XIII) was obtained in 75% yield as brilliant golden flakes, m. p. 288°, from pyridine (Found : C, 47·2; H, 4·1; N, 6·65. $C_{33}H_{34}O_7N_4S_5Se$ requires C, 47·3; H, 4·05; N, 6·7), $\lambda_{max.}$ 765 mμ in pyridine.

3-Ethoxycarbonylmethyl-2-[2-(3-ethoxycarbonylmethyl-4-oxo-2-thiothiazolidin-5-ylidene)-2-ethylthioethylidene]-5-{2-[4-(3-ethylbenzoselenazolin-2-ylidene-ethylidene)-5-oxo-3-methylthiazolidin-2-ylidene]-1-ethylthioethylidene}thiazolid-4-one (XII) was obtained in 73% yield and formed dark, bronze threads, m. p. 260°, from pyridine–ethanol (Found : C, 47·95; H, 4·35; N, 6·0; S, 20·5. $C_{37}H_{40}O_7N_4S_6Se$ requires C, 48·1; H, 4·35; N, 6·05; S, 20·8%), $\lambda_{max.}$ 832 mμ in pyridine.

3-Ethoxycarbonylmethyl-5-{2-[4-(3-ethylthiazolidin-2-ylidene-ethylidene)-5-oxo-3-methylthiazolidin-2-ylidene]-1-ethylthioethylidene}-2-[2-ethylthio-2-(2-ethylthio-5-oxothiazolin-4-ylidene)ethylidene]thiazolid-4-one (XI; R = R′ = SEt) obtained in 62% yield formed flat, golden needles, m. p. 243°, from pyridine–ethanol (Found : N, 7·35; S, 29·05. $C_{31}H_{38}O_5N_4S_7$ requires N, 7·25; S, 29·1%), $\lambda_{max.}$ 782 mμ in pyridine.

3-Ethoxycarbonylmethyl-2-[2-ethoxy-2-(2-ethylthio-5-oxothiazolin-4-ylidene)ethylidene]-5-{2-4-(3-ethylthiazolidin-2-ylidene-ethylidene)-5-oxo-3-methylthiazolidin-2-ylidene]-1-ethylthioethylidene}-thiazolid-4-one (XI; R = SEt, R′ = OEt), obtained in 87·5% yield, formed tiny golden flakes, m. p. 228°, after recrystallization from benzene, then from pyridine–ethanol (Found : N, 7·3; S, 25·3. $C_{31}H_{38}O_6N_4S_6$ requires N, 7·45; S, 25·5%), $\lambda_{max.}$ 744 mμ in pyridine.

RESEARCH LABORATORIES,
KODAK LIMITED, HARROW, MIDDLESEX.

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Structural Studies of the Cellulose Synthesised by Acetobacter acetigenum.*

By K. S. BARCLAY, E. J. BOURNE, M. STACEY, and M. WEBB.

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The nitrogen-free polysaccharide synthesised from D-glucose by cultures of *Acetobacter acetigenum* (T. K. Walker's strain) has been proved to be a cellulose, in agreement with Kaushal and Walker (*Biochem. J.*, 1951, **48**, 618). Methylation and end-group assay revealed the average chain length of its trimethyl ether to be of the order of 600 glucose units. The relative merits of the Barnett and the acetic acid–trifluoroacetic anhydride method of acetylation have been compared. Membranes produced by resting cells of the organism from D-glucose and from D-mannose have been shown to contain only D-glucose residues in the polysaccharide component.

ALTHOUGH it has been known for more than twenty years that the polysaccharide constituent of the membrane produced by *Acetobacter xylinum* is a cellulose (cf. Eggert and Luft, *Z. physikal. Chem.*, 1930, **7**, *B*, 468; Hibbert and Barsha, *Canad. J. Res.*, 1931, **5**, 580; 1934, **10**, 170), it was not until 1951 that Kaushal and Walker (*Biochem. J.*, 1951, **48**, 618) reported the first structural studies of the water-insoluble polysaccharide of the membrane of *Acetobacter acetigenum*. These authors showed that acetolysis yielded cellobiose octa-acetate and α- and β-D-glucose penta-acetate, while acetylation afforded a triacetate, and

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they concluded that the polysaccharide concerned was a cellulose. We now present more detailed evidence which confirms this conclusion.

Acetobacter acetigenum (T. K. Walker's strain) grows well on media containing ammonium sulphate 0·3%, potassium dihydrogen phosphate 0·3%, magnesium sulphate 0·2%, ethanol 2·0%, D-glucose 2·0%, and either Marmite 0·5% (Medium A), or calcium pantothenate and riboflavin (10^{-5}%, each) (Medium B). In most of the experiments described, medium (A) was employed. The membranes from many such cultures, after being pulped and extracted with 5% sodium hydroxide solution, gave a fibrous white polysaccharide, which was free from nitrogenous contaminants and gave analyses correct for a hexosan. Acetolysis with acetic anhydride–sulphuric acid afforded a mixture of acetates; on deacetylation of this and filter-paper chromatography, glucose and cellobiose were the only sugars detected. Crystallisation of the bulk of the acetate mixture gave crystalline α-cellobiose octa-acetate.

The polysaccharide was methylated with sodium and methyl iodide in liquid ammonia at −70°, essentially as described by Freudenberg and Boppel (*Ber.*, 1938, **71**, 2505). The methyl ether (OMe, 44·3%, compared with 45·6% for a tri-*O*-methylhexosan) had $[\alpha]_D$ −5·75° in chloroform, which agreed well with the values (−5·0°, −4·0°, −8·0°) recorded by Haworth, Hirst, Owen, Peat, and Averill (*J.*, 1939, 1885) for various tri-*O*-methylcelluloses. Paper-chromatographic analysis of a hydrolysate showed only one spot; this had an R_F value and staining reactions identical with those of 2 : 3 : 6-tri-*O*-methyl-D-glucose. Indeed, this sugar was subsequently isolated in crystalline form from the hydrolysate. Repeated extractions of the hydrolysate with chloroform under carefully controlled conditions yielded a syrup, in which 2 : 3 : 4 : 6-tetra-*O*-methylglucose also could be detected. Quantitative analysis of this syrup on filter-paper (Hirst, Hough, and Jones, *J.*, 1949, 928) disclosed 0·88 mole of tetraether per mole of triether. From the known partition coefficients of these components between chloroform and water (Macdonald, *J. Amer. Chem. Soc.*, 1937, **59**, 1503), the average chain length of the tri-*O*-methylpolysaccharide was calculated to be of the order of 600 glucose units. If the polysaccharide ether were unbranched, this would represent also the number-average degree of polymerisation. Thus the bacterial polysaccharide was proved to be a cellulose, in which β-D-glucopyranose units were linked through positions 1 and 4 to give long, essentially unbranched, chains, probably having an average molecular weight somewhat higher than was found, after methylation, in the trimethyl ether.

A sample of the bacterial cellulose was acetylated by Barnett's method (*J. Soc. Chem. Ind.*, 1921, **40**, 8), and another by treatment with acetic acid–trifluoroacetic anhydride (Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976; Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942). Each acetate was deacetylated catalytically with sodium methoxide, and then re-acetylated by the method employed initially. The molecular weights of the four acetates thus obtained were compared by viscosity measurements (see Table). It was confirmed that very extensive degradation had occurred during

Molecular weights of cellulose acetates

Method of acetylation	$[\eta]$	D.P.
Barnett	0·11	21
Barnett (repeat)	0·09	17
$CH_3{\cdot}CO_2H$–$(CF_3{\cdot}CO)_2O$ (2 expts.)	4·75, 2·00	900, 380

acetylation by Barnett's process, whereas only about one bond per thousand was broken by acetic acid–trifluoroacetic anhydride. Such a result was not unexpected since it had been shown already (Bourne, Stacey, Tatlow, and Tedder, *loc. cit.*) that the latter process gives a good yield of the octa-acetate from so acid-labile a carbohydrate as sucrose. The acetates produced by acetic acid–trifluoroacetic anhydride were fibrous, whereas those resulting from the Barnett process were powders. However, the acetyl contents of the products from the trifluoroacetic anhydride procedure were *ca.* 2% lower than the theoretical figure, possibly owing to the introduction of a few trifluoroacetyl groups, which would be removed subsequently during the purification stage.

During the two years which have elapsed since the above work was completed, it has become possible to distinguish between α- and β-linked polyglucosans by determinations of infra-red spectra over the frequency range 730—960 cm.$^{-1}$ (Barker, Bourne, Stacey, and Whiffen, *Chem. and Ind.*, 1953, 196; *J.*, 1954, 171). Bacterial cellulose showed absorption peaks at 766, 894, 914, and 933 cm.$^{-1}$, and identical peaks were given by cotton cellulose. The absorption peak at 894 cm.$^{-1}$ is given by all β-anomers examined in the glucose series, including the cello-dextrins; there was no peak at *ca.* 840 cm.$^{-1}$, at which frequency the α-anomers show absorption.

The abilities of *Acetobacter acetigenum* and *A. xylinum* to grow on various substrates have been compared; these substrates were used instead of D-glucose in the synthetic medium (B). Whereas *Acetobacter acetigenum*, at the fourth sub-culture, could utilise ammonium lactate, methyl α-D-glucopyranoside, and dipotassium α-D-glucose 1-phosphate, none of these compounds supported the growth of *Acetobacter xylinum*. It follows that the former organism has a more complete cellulose-synthesising enzyme system than the latter. This confirms Kaushal and Walker's finding (*loc. cit.*), that *A. acetigenum*, but not *A. xylinum*, can utilise methyl α- and β-D-glucopyranoside, three pentoses, erythritol, and ethylene glycol.

Resting cells of *A. acetigenum* produced membranes when incubated with either D-glucose or D-mannose in phosphate buffer. After purification, each membrane was submitted to acetolysis, and the product was deacetylated, before being examined on a paper chromatogram. In each case, spots were observed which corresponded to reference spots of glucose and cellobiose. Thus the cells have the ability to convert D-mannose into derivatives of glucose.

When a suspension of the cells in phosphate buffer was shaken with glass beads, it was rendered non-viable and 95—99% of the cells were ruptured. The supernatant liquid produced no cellulose from D-glucose, whereas there was synthesis when a suspension of the cell debris in fresh phosphate buffer was incubated with D-glucose. It seems, therefore, that the enzyme(s) responsible for cellulose synthesis remained bound to the cell debris and were not extra-cellular.

Experimental

Nutrient Media.—Medium (A) contained ammonium sulphate (3·0 g.), potassium dihydrogen phosphate (3·0 g.), magnesium sulphate heptahydrate (2·0 g.), Marmite (5·0 g.), glucose (20 g.), ethanol (20 ml.), and water (1000 ml.) (cf. Henneberg, " Handbuch der Gärungsbakteriologie," Parey, Berlin, 1926). In medium (B), the Marmite was replaced by calcium pantothenate (0·10 mg.) and riboflavin (0·10 mg.).

Synthesis and Purification of Cellulose.—The membranes formed in 7 days by numerous cultures of *Acetobacter acetigenum* (T. K. Walker's strain), grown on medium (A) at 30°, were pulped with water in a Waring blender, and the insoluble residue, collected on cheese-cloth, was treated with 5% sodium hydroxide solution at 30° for 18 hr. The cellulose was collected, washed with water, and suspended in water, to which acetic acid was added at intervals until the solution remained acid to litmus for 12 hr. After being dialysed against distilled water, the stock cellulose sample (18 g.) was freeze-dried [Found: C, 44·1; H, 7·0; N, 0. Calc. for $(C_6H_{10}O_5)_n$: C, 44·5; H, 6·2%].

Infra-red Analysis.—The infra-red spectrum of the stock cellulose sample, determined over the frequency range 730—960 cm.$^{-1}$, by the " Nujol "-mull technique, showed absorption peaks at 766, 894, 914, and 933 cm.$^{-1}$ (cf. Barker, Bourne, Stacey, and Whiffen, *loc. cit.*).

Acetolysis of the Stock Cellulose Sample.—The cellulose (1·00 g.) was added in small portions, with vigorous stirring, to a mixture of acetic anhydride (3·80 ml.) and concentrated sulphuric acid (0·40 ml.), the temperature being kept below 5° during the addition and for several hours afterwards. Then, acetic anhydride (1·00 ml.) was added, and the mixture was kept at room-temperature for 24 hr., and subsequently at 85° for 14 min. It was cooled and poured into ice-water (100 ml.). The precipitate (X; 1·50 g.) was collected, washed, and dried. The bulk of the material (1·40 g.) was extracted with hot ethanol, and the filtered extract was evaporated under diminished pressure. The residue, crystallised from chloroform–methanol, gave α-cellobiose octa-acetate (0·63 g.), m. p. 224°, $[\alpha]_D^{20}$ +41·6° (*c*, 0·96 in $CHCl_3$) (Found: C, 49·7; H, 5·8;

Ac, 50·5. Calc. for $C_{28}H_{38}O_{19}$: C, 49·6; H, 5·6; Ac, 50·7%). Hudson and Johnson (*J. Amer. Chem. Soc.*, 1915, **37**, 1276) reported m. p. 229°, $[\alpha]_D^{20}$ +42·0° (in $CHCl_3$).

The remainder (0·10 g.) of precipitate (X) was treated, in chloroform (5 ml.)–methanol (2 ml.), with a trace of sodium methoxide at room temperature for 24 hr. The solvents were removed at 20°/12 mm., and the residue was dissolved in water, freed from ions, and freeze-dried. A paper chromatogram of the product, irrigated with the upper layer of a mixture of *n*-butanol (40%), ethanol (10%), water (49%), and ammonia (1%), and sprayed with Partridge's aniline hydrogen phthalate reagent (*Nature*, 1949, **164**, 443), showed two components, having R_F values identical with those of cellobiose and glucose reference spots.

Methylation of the Stock Cellulose Sample.—The cellulose (6·30 g.) was methylated with sodium and methyl iodide in liquid ammonia at −70°, essentially as described by Freudenberg and Boppel (*loc. cit.*). The treatment was repeated thrice more, the product being isolated at each stage. The product obtained finally when the ammonia was removed was suspended in water, dialysed against distilled water until free from iodide, and freeze-dried to give the crude polysaccharide ether (3·66 g.) (Found: ash, 3·4; OMe, 40·3. Calc. for tri-*O*-methylcellulose: OMe, 45·6%). This material was extracted (Soxhlet) with ether for 3 hr., and then dissolved in chloroform. The solution was clarified in the centrifuge, and evaporated under diminished pressure at room temperature from beneath a layer of water. The cellulose ether (2·46 g.), recovered when the aqueous suspension was freeze-dried, had $[\alpha]_D^{20}$ −5·75° (*c*, 0·69 in $CHCl_3$) [Found: ash, 2·7; OMe, 43·1% (44·3% when corrected for ash)].

End-Group Assay.—The methylated cellulose (1·004 g.) was dissolved in chloroform (15 ml.), mixed with 8% methanolic hydrogen chloride (15 ml.), and heated at 100° (sealed tube) for 8 hr. The solvents were removed under diminished pressure at 20°, and the residue was dissolved in 4% hydrochloric acid (85 ml.). The solution was kept at 100° for 5 hr., neutralised with silver carbonate, and filtered; the last traces of silver were removed with hydrogen sulphide. The syrup obtained when the solution was evaporated at 40°/12 mm. was dissolved in water (10 ml.), and the solution was extracted with chloroform (9 × 10 ml.); each extraction was continued for 30 min. to ensure equilibration. The combined chloroform extracts were shaken with an equal volume of water at intervals during 45 min. The chloroform layer was separated, and concentrated at 30° to a syrup, which was redissolved in water (0·5 ml.).

Paper-chromatographic examination of the final aqueous solution showed only two components; these had R_F values identical with those of reference spots of 2 : 3 : 6-tri-*O*-methyl- and 2 : 3 : 4 : 6-tetra-*O*-methyl-glucose. Quantitative paper-chromatographic analysis, essentially as described by Hirst, Hough, and Jones (*loc. cit.*), but with minor modifications introduced by Bebbington, Bourne, and Wilkinson (*J.*, 1952, 246), revealed the molar ratio of "tetra" to "tri" to be 0·88. On the basis of the partition coefficients between chloroform and water given by Macdonald (*loc. cit.*), the factors 1·62 and 825 were applied to give the molar ratio of "tetra" to "tri" in the hydrolysate of the tri-*O*-methylcellulose; this corresponded to an average chain length of the order of 600 glucose units.

Isolation of 2 : 3 : 6-*Tri*-O-*methylglucose.*—The aqueous layer remaining from the above chloroform extractions was concentrated to a syrup, which crystallised from ethyl acetate to give 2 : 3 : 6-tri-*O*-methyl-α-D-glucose (0·63 g.), m. p. and mixed m. p. 115°, $[\alpha]_D^{20}$ +70·2° (equil.; *c*, 0·97 in H_2O) (Found: C, 48·7; H, 8·2; OMe, 41·3. Calc. for $C_9H_{18}O_6$: C, 48·6; H, 8·2; OMe, 41·9%).

Acetylation of the Stock Cellulose Sample.—(a) *By Barnett's method.* The dry cellulose (1·00 g.), treated with acetic acid, acetic anhydride, chlorine, and sulphur dioxide, as described by Irvine and Hirst (*J.*, 1922, **121**, 1585), gave the acetate (1·59 g.) (Found: Ac, 44·6. Calc. for tri-*O*-acetylcellulose: Ac, 44·8%). A portion (0·80 g.) of the acetate was deacetylated with a trace of sodium methoxide in chloroform–methanol at room temperature for 24 hr. Acetone was added to diminish the density of the liquid phase, and the cellulose was collected in the centrifuge, washed with acetone, and then with water, and dried. Reacetylated as before, it gave an acetate (0·80 g.) (Found: Ac, 44·7%).

The acetyl contents were determined by Clark's method (*Ind. Eng. Chem. Anal.*, 1936, **8**, 487; 1937, **9**, 539).

(b) *By acetic acid–trifluoroacetic anhydride.* The dry cellulose (0·86 g.) was stirred with dry acetic acid (13·3 ml.) and trifluoroacetic anhydride (21·0 ml.) at room temperature for 4 hr. (cf. Bourne, Stacey, Tatlow, and Tedder, *loc. cit.*). Dry light petroleum (30 ml.; b. p. 60—80°) was added, and stirring was continued for 15 min., before the precipitate was collected and washed repeatedly with light petroleum. Chloroform (50 ml.) was added and removed by distillation under diminished pressure, a procedure which was repeated six times to remove any residue of

the acetylating reagents. A solution of the product in chloroform (100 ml.), clarified in the centrifuge, was poured into dilute sodium hydrogen carbonate solution, and the chlorofrom was removed by distillation under diminished pressure at room temperature. The precipitate was filtered off, thoroughly washed with water, and dried, to give the acetate (1·40 g.) (Found : Ac, 42·9%).

A portion (0·80 g.) of this material, deacetylated as above, and then re-treated with acetic acid–trifluoroacetic anhydride, gave an acetate (0·80 g.) (Found : Ac, 42·6%).

Viscosity Measurements on the Cellulose Acetate Samples.—A modified Ubbelohde viscometer of the type described by Davis and Elliott (*J. Colloid Sci.*, 1949, **4**, 313) was used to measure viscosities of chloroform solutions of the acetates. The procedure was as described by Gilbert, Graff-Baker, and Greenwood (*J. Polymer Sci.*, 1951, **6**, 585). The intrinsic viscosities $[\eta]$, obtained by extrapolation to infinite dilution of the graph of $\eta_{sp.}/c$ against c (in g. per 100 ml.), are shown in the Table. Staudinger and Werner's constant ($K = 5{\cdot}3 \times 10^{-4}$ base mole $l.^{-1}$; *Ber.*, 1937, **70**, 2140) was used to give the degrees of polymerisation.

Acetolysis of Membranes produced by Resting Cells of Acetobacter acetigenum.—(a) *From glucose.* Membranes from cultures of *A. acetigenum*, which had been grown for 7 days on medium (A), were washed thoroughly with water, suspended in water, and pulped in a Waring blender. The suspension was filtered through cheese-cloth, which retained the bulk of the cellulose but allowed the cells to pass through; they were collected in the centrifuge and washed again with water (cf. Aschner and Hestrin, *Nature*, 1946, **157**, 659). The resting cells were suspended in 0·2M-phosphate buffer (pH 5·6; 30 ml.), and a portion (1 ml.) of the suspension was added to each of 25 Petri dishes containing a 2% solution (20 ml.) of glucose. After incubation at 37° for 24 hr., the membranes produced were washed, purified by treatment with sodium hydroxide, and submitted to acetolysis, as described above. The crude product obtained on pouring the acetolysis mixture into water was deacetylated and examined on a paper chromatogram; two spots appeared, having R_F values identical with those of glucose and cellobiose.

(b) *From mannose.* The experiment was repeated with mannose instead of glucose in the Petri dishes. The deacetylated product showed glucose and cellobiose, but no mannose, on a paper chromatogram; after hydrolysis with acid, it showed only glucose.

Cellulose Synthesis by Cell Debris.—A thick suspension of resting cells in 0·2M-phosphate buffer (pH 5·6; 5 ml.) was shaken with glass beads (0·5 mm. diameter) in a Mickle shaker for 10 periods of 2 min., with intervals of 3 min. (to avoid over-heating). Staining tests indicated that 95—98% of the cells were disrupted. The cell debris was suspended in 0·2M-phosphate buffer (pH 5·6; 5 ml.), and when a test portion (1 ml.) of the suspension was incubated with a 2% solution (10 ml.) of glucose at 37° for 20 hr. cellulose was produced. On the other hand, the supernatant liquid (2 ml.) gave no cellulose when tested in the same way.

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CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

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Constituents of the Seeds of Corchorus olitorius, *L. Part II.* Isolation of β-Sitosterol and Corchorolic Acid.*

By Gabra Soliman and Wahba Saleh.

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β-Sitosterol occurs in the seeds of *Corchorus olitorius* and *C. capsularis*. The sterol isolated from the Indian jute seeds and claimed to be new was not found in the Egyptian varieties. The yellow substance obtained from the alcoholic extract of the seeds proved to be a mixture of a phenol and an aliphatic hydroxy-acid, corchorolic acid, $C_{26}H_{52}O_3$, which gave on oxidation a dicarboxylic acid, $C_{26}H_{50}O_4$.

In conformity with our previous publication * regarding the identity of corchorin with strophanthidin, Chaudhury and Dutta (*J. Indian Chem. Soc.*, 1951, **28**, 167) reported the isolation of corchorin from the Indian jute seeds by a simplified process. Furthermore, they have prepared the acetate of this genin and found that it has the melting point and optical rotation recorded by us. This reveals no difference between the Egyptian and the Indian varieties of *Corchorus*.

Sen (*ibid.*, 1928, **5**, 759) found the oil of the seeds of *Corchorus capsularis* to contain a phytosterol, m. p. 128°. Sen and Chakravarti recently (*ibid.*, 1951, **28**, 727) purified this sterol and characterised it as a new sterol, $C_{29}H_{50}O$, having an acetate, m. p.122°, a benzoate, m. p. 139°, and a digitonide, m. p. 215—220° (decomp.).

In our search for other constituents in the seeds of *C. olitorius*, we hydrolysed its oil and isolated a phytosterol : the composition of the oil of this variety and the presence of a mixture of sterols had earlier been reported by Sen and Chakravarti (*ibid.*, p. 390). Our sterol was readily identified as β-sitosterol, m. p. 139°, and was characterised as the acetate, m. p. 128°, benzoate, m. p. 147°, and 3 : 5-dinitrobenzoate, m. p. 203°, the identities being established by comparison with authentic specimens (Wallis and Chakravorti, *J. Org. Chem.*, 1937, **2**, 335). Similarly, we have isolated β-sitosterol from the oil of *C. capsularis* of an Egyptian origin (*J.*, 1950, 2199, footnote).

Contrary to expectation, we have failed to isolate Sen and Chakravarti's sterol alongside our β-sitosterol. The absence of this new sterol from the two Egyptian varieties of *Corchorus*, and the absence of β-sitosterol from the Indian jute seeds cannot be reconciled if only due to climatic factors.

In our previous publication (*loc. cit.*) we described a yellow phenol. Attempts to purify this substance by repeated crystallisations led to a gradual fading of its colour and disappearance of its phenolic reaction. However, when its solution in ethyl acetate was shaken with aqueous sodium hydrogen carbonate, a water-insoluble sodium salt of an acid separated. The free acid, m. p. 96°, gave a negative test with ferric chloride and behaved as if it were a saturated aliphatic compound. In another procedure, the crystalline sodium salt was obtained by the action of hot sodium hydroxide solution on the yellow substance. In the same way this acid, now named corchorolic acid, was also isolated from the seeds of *C. capsularis*. Analysis, titration, and acetylation indicate a formula $C_{26}H_{52}O_3$ including a free carboxyl group and a primary or secondary hydroxyl group. Esters were obtained by the action of diazomethane, or of methanol or ethanol and sulphuric acid; analyses of the esters and their acetyl derivatives agree with the proposed formula, but the next lower and higher homologues are not entirely excluded.

The ease of esterification of corchorolic acid and the ready hydrolysis of its esters indicate that the carboxyl group is not attached to a tertiary atom; the stability of methyl corchorolate towards heat in a high vacuum is further evidence that the hydroxyl group is not tertiary. On the other hand, oxidation of corchorolic acid, *via* the methyl ester, with chromium trioxide to a dicarboxylic acid, $C_{26}H_{50}O_4$, m. p. 115°, shows that the hydroxyl

* Part I, *J.*, 1950, 2198.

group is primary. Moreover, the optical inactivity of corchorolic acid and its derivatives might lead to the assumption that its two functional groups are attached to the ends of a normal paraffin chain. This, however, would necessitate the identity of its oxidation product with tetracosane-1 : 24-dicarboxylic acid, m. p. 123·5° (corr.) (Fairweather, *Proc. Roy. Soc. Edinb.*, **1926**, **21**, 71) : we are as yet unable to confirm this, and the melting points differ considerably.

Experimental

Isolation of β-Sitosterol.—The oil (200 g.) obtained by extraction of the seeds of *C. olitorius* with light petroleum (b. p. 60—80°) was hydrolysed by 4 hours' boiling with 20% alcoholic potassium hydroxide (500 ml.). Most of the alcohol was then distilled off and the residue dissolved in water and extracted with ether. The ethereal solution yielded 6 g. of unsaponifiable matter from which 3·5 g. of the crude sterol, m. p. 105°, were obtained after washing with cold methanol. It crystallised from acetone in plates, m. p. 122—125°. On concentration of the methanol washings or the acetone mother-liquor, the same sterol contaminated with waxy impurities was recovered. The wax was removed by digestion with warm light petroleum (b. p. 40—60°). The insoluble residue, m. p. 135°, crystallised from ethanol in plates, m. p. 139°, $[\alpha]_D^{22}$ −27·5° (*c*, 2·77 in $CHCl_3$), identical with β-sitosterol prepared fron cotton-seed oil (Wallis and Chakravorti, *loc. cit.*). It gave an acetate which crystallised from methanol in plates, m. p. and mixed m. p. 128° (Found : C, 81·6; H, 11·3. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·5%), $[\alpha]_D^{22}$ −37·6° (*c*, 1·95 in $CHCl_3$), a benzoate, plates (from benzene–methanol), m. p. and mixed m. p. 147°, $[\alpha]_D^{22}$ −11·22° (*c*, 2·84 in $CHCl_3$) (Found : 83·2; H, 10·3. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5%), and a 3 : 5-dinitrobenzoate (prepared by 3 : 5-dinitrobenzoyl chloride in pyridine), pale yellowish plates (from benzene–methanol), m. p. and mixed m. p. 203°.

On hydrolysis of the esters with alcoholic potassium hydroxide, β-sitosterol, m. p. 139°, was recovered.

β-Sitosterol was also isolated from the seeds of *C. capsularis* when 100 g. of the oil were saponified as described before. The unsaponifiable matter (3 g.) yielded the crude sterol, m. p. 105°, on treatment with cold methanol. The pure sterol crystallised from ethanol in plates, m. p. 139°, $[\alpha]_D^{22}$ −28·3° (*c*, 2·84 in $CHCl_3$). It gave an acetate, m. p. 128°, $[\alpha]_D^{22}$ −33·9° (*c*, 2·34 in $CHCl_3$) (Found : C, 81·3; H, 11·2. Calc. for $C_{31}H_{52}O_2$: C, 81·6; H, 11·3%), a benzoate, m. p. 147°, and a 3 : 5-dinitrobenzoate, m. p. 203°, all identical with authentic specimens. No other sterol besides β-sitosterol could be obtained from the solvents used in purification or crystallisation.

Isolation of Corchorolic Acid.—The yellowish-brown product (300 g.) obtained from the alcoholic extract (Soliman and Saleh, Part I) of the de-fatted meal (5 kg.) of the seeds of *C. olitorius* was refluxed with ethyl acetate, and the extract was separated by decantation. This process was repeated twice and, after cooling, a sticky brown material separated. The mother-liquor yielded on concentration a yellow solid (80 g.) which was redissolved in ethyl acetate. The solution was decanted from the gummy residue and refluxed with charcoal. The filtrate deposited, on cooling, a yellow micro-crystalline solid, m. p. 103—105°, which gave a green colour with ferric chloride and a yellow colour with potassium hydroxide. It is sparingly soluble in ether or benzene, and dissolves in hot methanol, ethanol, or chloroform, and separates on cooling in a gelatinous form.

Corchorolic acid could not be freed entirely from the phenolic component by repeated crystallisations from ethyl acetate or benzene. When a solution of the yellow solid in ethyl acetate was extracted with sodium hydrogen carbonate solution, sodium corchorolate separated as a jelly. The phenolic component was recovered from the solvent as a yellowish-brown solid. After separation and washing, sodium corchorolate was dissolved in hot dilute acetic acid and heated with charcoal. On cooling of the filtrate, *corchorolic acid* separated as a flocculent precipitate. Crystallised from ethyl acetate it had m. p. 96°, gave a negative test with ferric chloride, and did not decolorise bromine solution in acetic acid. Its solution in pyridine showed no rotation [Found : C, 75·6, 75·5; H, 12·8, 12·6; CO_2H (titration), 11·0, 10·9%; *M* (Rast), 403. $C_{26}H_{52}O_3$ requires C, 75·7; H, 12·7; CO_2H, 10·9%; *M*, 412·4].

For the preparation of corchorolic acid in larger quantities, the yellow solid (20 g.) was boiled gently with 10% aqueous sodium hydroxide (80 ml.) for about 20 min., the mixture becoming brown, and sodium corchorolate (7 g.) separated in glistening fine plates. The acid was liberated and purified as before, and its solution in pyridine showed no rotation (Found : C, 75·6; H, 12·6%).

Acetylcorchorolic acid was prepared by the action of acetic anhydride and pyridine, and crystallised from benzene–light petroleum (b. p. 60—80°) in plates, m. p. 82—83° (Found: C, 74·3; H, 11·95; CO_2H, 9·3. $C_{28}H_{54}O_4$ requires C, 73·9; H, 12·0; CO_2H, 9·5%). Its solution in pyridine showed no rotation.

Methyl Corchorolate.—A suspension of the acid (2 g.) in ether was mixed with ethereal diazomethane and after 3 hr. the solution was washed with 2% aqueous sodium hydroxide and dried. The ester recovered from the ethereal solution crystallised from light petroleum (b. p. 40—60°) in small glistening plates, m. p. 83—84° (Found: C, 75·9, 75·55; H, 12·6, 12·8; OMe, 8·5. $C_{27}H_{54}O_3$ requires C, 76·0; H, 12·8; OMe, 7·3%). *Methyl corchorolate* (same m. p.) was also obtained when the acid (2 g.) in methanol (50 ml.) and concentrated sulphuric acid (3 ml.) was refluxed for 3 hr. It was completely hydrolysed by hot 5% alcoholic potassium hydroxide in 2 hr., the acid melting at 96°. Methyl corchorolate was recovered unchanged after 1 hr. in a high vacuum at 120—125°.

Methyl acetylcorchorolate, prepared as usual, crystallised from light petroleum (b. p. 40—60°) in glistening plates, m. p. 74° (Found: C, 74·7; H, 12·1. $C_{29}H_{56}O_4$ requires C, 74·3; H, 12·05%). It showed no rotation in a benzene solution.

Ethyl Corchorolate.—The acid (1 g.) was refluxed in absolute alcohol (30 ml.) and concentrated sulphuric acid (1·5 ml.) for 3 hr. The *ester* crystallised from light petroleum (b. p. 40—60°) in plates, m. p. 78° (Found: C, 76·7, 76·6; H, 12·6, 13·05. $C_{28}H_{56}O_3$ requires C, 76·3; H, 12·8%). It showed no rotation in benzene solution. Its *acetate* crystallised from light petroleum in plates, m. p. 63—64° (Found: C, 74·9; H, 12·2. $C_{30}H_{58}O_4$ requires C, 74·6; H, 12·1%).

Oxidation of Methyl Corchorolate.—A solution of the ester (2 g.) in hot acetic acid (100 ml.) was cooled to 40°, the ester separating in a gelatinous form. To this mixture, chromium trioxide (2 g.) in acetic acid (40 ml.) and water (2 ml.) was gradually added with stirring, at <40°. Stirring was continued for 3 hr. and the mixture was then kept for about 12 hr. at room temperature, poured into water, and extracted with chloroform. Subsequently, the chloroform solution was extracted with 2% aqueous sodium hydroxide; the sodium salt of the acid ester separated at the interface. The salt was dissolved in hot acetic acid and the solution boiled with charcoal. The filtrate deposited, on cooling, the acid ester (0·8 g.) in plates, m. p. 80—85°. The chloroform solution yielded 0·3 g. of the methyl ester which escaped oxidation.

The acid ester was heated with 10% alcoholic potassium hydroxide for 2 hr. After distillation of the alcohol, the dipotassium salt was separated and acidified with acetic acid. The *dicarboxylic acid* crystallised from acetic acid and recrystallised from ethyl acetate in plates, m. p. 115° [Found: C, 73·5; H, 12·1; CO_2H (titration), 21·3. $C_{26}H_{50}O_4$ requires C, 73·2; H, 11·8; $2CO_2H$, 21·1%]. Its *dimethyl ester*, prepared by diazomethane, crystallised from light petroleum (b. p. 40—60°) in plates, m. p. 69° (Found: C, 74·0; H, 12·1; OMe, 14·9. $C_{28}H_{54}O_4$ requires C, 73·9; H, 12·0; 2OMe, 13·7%). On hydrolysis, the dicarboxylic acid, m. p. 115°, was regenerated.

Corchorolic acid was also separated from the seeds of *C. capsularis* when the yellow substance obtained from its alcoholic extract was analogously treated, but the yield was rather poor.

Chemistry Department, Faculty of Science, Alexandria University,
Moharram Bey, Alexandria. [*Received, December* 21*st*, 1953.]

Exchange Reactions of Solid Oxides. Part III. Magnesium Oxide.*

By G. Houghton and E. R. S. Winter.

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Exchange of ^{18}O between the surface of magnesium oxide and oxygen gas has been studied over the temperature range 370—510°, oxygen pressures of 1—14 cm. being used. The rate of exchange and the amount of exchangeable oxide surface depend on the previous outgassing treatment of the oxide. The exchange process has an activation energy of approx. 3 ± 2 kcal. mole^{-1} above 420—450° (depending on temperature of outgassing) and 34 ± 2 kcal. mole^{-1} below this temperature. An alternative treatment of the kinetics gives E for the high-temperature process of $7{\cdot}7 \pm 2$ kcals. mole^{-1} and for the lower temperature range approximately 36 ± 2 kcal. mole^{-1}. Rates of adsorption of oxygen by magnesium oxide at pressures near 10^{-3} cm. show that at low pressures the initial adsorption has an activation energy of about 14 kcal. mole^{-1}, but it is not possible with certainty to extrapolate to higher pressures and the nature of the rate-determining step in the two exchange processes remains uncertain.

Earlier papers (Houghton and Winter, *Nature*, 1949, **164**, 1130; Winter, *J.*, 1950, 1170; Winter, *Discuss. Faraday Soc.*, 1950, **8**, 231; Houghton and Winter, "Mass Spectrometry," Inst. of Petroleum, 1952, p. 127) have described the technique used to study the exchange of ^{18}O between enriched oxygen gas and finely-divided oxides: some discussion has also been given of the kinetics of the process. This paper reports a detailed investigation of the exchange with magnesium oxide: a study has been made of the effect upon the kinetics of varying the time and temperature of outgassing, the temperature of the exchange reaction, and the oxygen pressure. It must be emphasised that this work is concerned with the initial rapid exchange reaction, associated with the surface of the oxide (Houghton and Winter, *Nature, loc. cit.*). A few of these observations have been given elsewhere, and the earlier values for velocity constants in some cases differ slightly from those now quoted; this is due to a more careful evaluation of α_0 and α_∞ (see *idem, ibid.*). In an attempt to identify the rate-determining step in the exchange, some measurements of the rate of adsorption of oxygen are reported here.

Experimental

Materials.—Magnesium oxide was of "AnalaR" purity, made by igniting the carbonate in air at 800° for *ca.* 4 hr. The oxygen, containing about 1·2% of ^{18}O, was prepared by electrolysis and was from the same stock as that used in earlier work; normal oxygen used for adsorption measurements was obtained by heating "AnalaR" potassium permanganate *in vacuo*; the first 10% of gas was rejected, and a middle fraction collected after passage through a trap cooled to −78°. Helium used in the adsorption experiments was from the British Oxygen Company, spectroscopically pure, and was passed through a trap at −78° before use.

Results.—Experiments designed to show the effect of time and temperature of outgassing, and pressure of oxygen, p_{O_2}, in the reaction system, are summarised in Tables 1—3. It is evident that the rate of reaction at a fixed temperature is strongly dependent upon the first two variables, but is not very sensitive to p_{O_2}. In the later work these three conditions were kept approximately constant in order to study the effect of reaction temperature upon the rate constant, k_0, and the exchangeable surface oxygen, n_s (atoms/g. of oxide). These experiments are summarised in Table 4 and Figs. 1 and 2, and yield the following rate equations, where X and X' refer to the left-hand portion of the upper and the lower curve in Fig. 2 respectively and Y and Y' to the right-hand portions.

$$X,\ k_0 = 0{\cdot}15 \exp(-2400/\boldsymbol{RT}) \quad (1)$$

$$Y,\ k_0 = 4{\cdot}25 \times 10^9 \exp(-35{,}400/\boldsymbol{RT}) \quad (2)$$

$$X',\ k_0 = 0{\cdot}12 \exp(-3000/\boldsymbol{RT}) \quad (3)$$

$$Y',\ k_0 = 1{\cdot}62 \times 10^8 \exp(-33{,}000/\boldsymbol{RT}) \quad (4)$$

* *J.*, 1950, 1170, 1175, are regarded as Parts I and II.

These equations are of the usual general form $k_0 = A \exp(-E/RT)$: there is some uncertainty as to the exact values of A and E, owing to the scatter of the results; the figures given above are the most probable values and the limits are given in Table 5.* This uncertainty is

TABLE 1. *Dependence of* k_0 *and* n_s *upon time of outgassing.*

p_{O_2} (mm.)	Outgassing conditions Time (hr.)	Temp.	Exchange reaction temp.	k_0, min.$^{-1}$	$n_s \times 10^{-20}$
75	14½	540°	442°	0·0276	5·88
75	18 + 7	540 445	442	0·0340	6·88
77	18	540	475	0·0278	6·95
79	18 +24	540 475	475	0·0403	8·91
142	18	533	533	0·118	7·95
92	1½	537	537	0·0365	10·2

TABLE 2. *Effect of temperature of outgassing upon* k_0 *and* n_s.

p_{O_2} (mm.)	Temp. Outgassing	Temp. Exchange	Outgassing time (hr.)	k_0, min.$^{-1}$	$n_s \times 10^{-20}$	$k_0 n_s \times 10^{-20}$
56	866°	460°	14	0·158	0·283	0·0447
89	748	461	13·8	0·087	1·70	0·149
85	640	459	13	0·045	2·99	0·135
87	600	463	14	0·042	3·96	0·167
69	540	459	17	0·0256	4·48	0·115
—	510	462	14	0·0155 *	6·90 *	0·107 *
76	866	388	13·8	—	0·183	—
101	540	388	14	0·00648	3·25	0·0211
62	510	388	14	0·00215	4·45	0·00957

* Interpolated.

TABLE 3. *Dependence of* k_0 *and* n_s *upon* p_{O_2}.

p_{O_2} (mm.)	Temp. Outgassing	Temp. Exchange	Outgassing time (hr.)	k_0, min.$^{-1}$	$n_s \times 10^{-20}$
41	510°	491°	14	0·0139	8·23
80	510	491	14	0·0160	8·15
83·5	510	493	14	0·0169	6·85
88	492	492	14	0·0149	—
147	492	492	14	0·0178	—
59	540	386	14½	0·0076	3·15
11·7	540	386	14	0·0069	5·15
101·5	540	388	14	0·0065	3·25
11·5	540	450	14	0·0383	6·30
67·5	540	450	15½	0·0324	—

regrettable but is due, we believe, to the extreme sensitivity of the oxide to the outgassing conditions; we were unable to control the temperature of the furnace to better than ±5° overnight. Recent work by Dr. J. A. Barnard upon zinc oxide (Thesis, London, 1952, and Part IV), which is more sensitive, has shown that by close control of the temperature (better than ±½° overnight) the scatter of the k_0 results is much reduced: it may be remarked, however, that the scatter of values of n_s (cf. Fig. 1) is not removed.

To provide an alternative measure of surface, low-temperature (78° K) nitrogen adsorption isotherms were measured for samples of the oxide which had been subjected to various outgassing treatments; these results are given in Table 6, calculated according to both the Harkins–Jura (*J. Chem. Phys.*, 1943, **11**, 430) and the Brunauer–Emmett–Teller (B.E.T.) (*J. Amer. Chem. Soc.*, 1938, **60**, 309) method. There is little difference between the surface areas given by the two theories, and we shall use the B.E.T. figures in discussion. Other results are given in Table 9.

* The method of least squares was applied to the results, giving equal weight to T and $\log k_0$; the limits were obtained from the quadratic mean error (cf. Whittaker and Robinson, "The Calculus of Observations," Blackie, Glasgow, 1946, p. 246).

TABLE 4. *The effect of exchange reaction temperature on* k_0 *and* n_s *for magnesium oxide at constant outgassing temperature.*

p_{O_2} (mm.)	Temp. Out-gassing	Temp. Exchange reaction	Out-gassing time (hr.)	k_0, min.$^{-1}$	n_s × 10^{-20}	p_{O_2} (mm.)	Temp. Out-gassing	Temp. Exchange reaction	Out-gassing time (hr.)	k_0 min.$^{-1}$	n_s × 10^{-20}
76·6	510°	507°	14	0·0194	10·6	67·9	540°	491°	16	0·0360	5·35
83·5	510	493	14	0·0169	6·85	76·9	540	475	18	0·0278	6·95
79·7	510	492	14	0·0160	8·15	72·1	540	462	13·5	0·0256	2·76
78·4	510	473	14	0·0150	7·46	69·0	540	459	17	0·0256	4·48
56·3	510	454	14	0·0159	5·4	67·5	540	450	15·5	0·0324	3·51
62·1	510	450	14	0·0163	5·76	74·9	540	442	14·5	0·0276	5·91
76·2	510	424	14	0·00804	5·40	78·1	540	419	13·5	0·0281	3·15
65·0	510	402	14	0·00347	5·20	78·0	540	403	14	0·0149	3·72
63·2	510	401	13·3	0·00293	3·35	56·1	540	397	14·5	0·0111	3·70
62·1	510	388	14	0·00215	4·45	59·3	540	386	14·5	0·00760	3·15
62·4	510	382	15	0·00148	6·26	100·0	540	382	13·5	0·00680	—
62·6	510	381	14	0·00132	5·07	61·6	540	368	14·5	0·00344	4·15
62·2	510	370	13·8	0·00112	5·00						

TABLE 5. *Accuracy of Arrhenius plots.*

Line	A	E	Line	A	E
X	0·022—1·0	2·4 ± 2·8	X'	0·036—0·42	3·0 ± 1·8
Y	(2·76—6·53) × 10^9	35·4 ± 0·6	Y'	3·2 × 10^7—1·0 × 10^9	33·0 ± 2·2

TABLE 6. *The surface areas of oxides by low-temperature nitrogen adsorption.*

Outgassing conditions Time (hr.)	Temp.	B.E.T.* C	m.²/g.	Harkins–Jura A	m.²/g.
32	400°	22·5	62·3	282·3	68·2
48	400	27·8	62·0	283·3	68·3
64	400	29·4	61·5	260·8	65·6
16	500	29·4	61·5	260·8	65·6
14·5	835	44·3	21·8	33·96	23·7

* The area of the nitrogen molecule is taken to be 16·2 Å².

TABLE 7.

p_{O_2} (mm.)	Outgassing conditions Time (hr.)	Temp.	Exchange reaction temp.	k_0, min.$^{-1}$
—	18	540°	540°	0·033 *
76·6	14	507	507	0·0194
87·7	14	492	492	0·0149
80·2	14	480	480	0·00924
86·4	14	444	444	0·00364

* Interpolated from Fig. 2.

TABLE 8. *Oxygen adsorption rates.*

Expt. No.	T	10^4 × Initial oxygen pressure, cm.	$(dn_g/dt)_{t=0}$ †	Expt. No.	T	10^4 × Initial oxygen pressure, cm.	$(dn_g/dt)_{t=0}$ †
A1	432°	10·8	0·30	A8	388°	10·6	0·19
A3	484	9·8	0·73	A9	416	11·2	0·24
A4	470	11·0	0·60	A11	412	10·8	0·23
A5	386	10·6	0·20	A2 *	432	9·0	0·45
A6	456	10·5	0·38	A10	416	27·0	0·42
A7	456	12·5	0·37	A12	486	20·2	1·05

* Run A1 allowed to come to equilibrium (24 hr.), final pressure being 2·3 × 10^{-5} cm., and another dose of oxygen added; this gave an equilibrium pressure of 3·3 × 10^{-5} cm. after 24 hr.

† To convert to atoms min.$^{-1}$ g.$^{-1}$ multiply by 3·07 × 10^{16}.

TABLE 9.

Outgassing temp.	Surface area, m.² g.$^{-1}$ B.E.T. at 78° K	Exchange at 460° C	Outgassing temp.	Surface area, m.² g.$^{-1}$ B.E.T. at 78° K	Exchange at 460° C	Outgassing temp.	Surface area, m.² g.$^{-1}$ B.E.T. at 78° K	Exchange at 460° C
866°	15·8 21·8	2·86	640°	33·9 32·2	30·2	600°	34·4	40·0
748	36·7	17·2				540	38·6	45·3
						510	61·5	69·7

Oxygen Adsorption Measurements.—The apparatus used was constructed from Pyrex glass and was of conventional design, comprising two McLeod gauges, covering the range 10^{-1} to 10^{-6} mm. (all pressures are expressed in mm. of Hg), a mercury manometer for measuring pressures above 10^{-1} mm., a dosing system, and bulbs containing pure dry oxygen and helium. The adsorption vessel was of approximately the same size as that used for the exchange reactions: the apparatus was interconnected with taps lubricated with Apiezon vacuum grease, and was evacuated through a cold trap at −78° with a two-stage mercury diffusion pump backed by a rotary oil-pump. Dead-space determinations were made by using helium, and included measurements of the equivalent dead-space of the adsorption vessel, loaded with oxide, at all temperatures used. In the latter case the pressure of helium was adjusted to be approximately that of the oxygen at equilibrium in the adsorption measurements; the connecting tubing was of 7 mm. internal diameter, and it was established by calculation that under these conditions of measurement corrections due to possible thermal transpiration were negligible. Fresh lots of oxide were used for each experiment.

The procedure was to outgas the oxide sample (usually 1 g.) overnight at 540°, as in the exchange experiments; if the vacuum in the morning was satisfactory ($<10^{-5}$ mm.) the oxide was isolated from the pumps and cooled to the desired temperature; when the temperature had been steady for about 20—30 min. the adsorption was begun: if the morning pressure was too high the experiment was abandoned. Preliminary work showed that the amount of adsorption was very small, amounting to about 6—9 × 10^{17} atoms/g., or about 0·1% of the exchangeable surface, at 485°, and 6 cm. upon 20 g. of magnesium oxide outgassed for 6 days to an ultimate pressure of 8 × 10^{-6} mm., at 535°: this corresponds to a pressure drop in the system of about 0·1 cm. in 6 cm.: under these conditions the adsorption appeared complete in less than 10 min. A similar experiment at 388° showed adsorption at 6 cm. pressure to be complete in, at the most, 5 min. It was, therefore, not possible to measure rates of adsorption at these pressures; such experiments were performed in the region of 10^{-2}—10^{-3} mm. Observations were made at constant volume by expanding a known quantity of oxygen from the gas-dosing system into the adsorption volume and measuring the pressure on one or other of the McLeod gauges after suitable time intervals. Most adsorptions were followed to equilibrium, but the process obeyed unambiguously no simple law, and it was most convenient to evaluate $(dn_g/dt)_{t=0}$, the initial uptake rate (n_g in atoms/g. of oxide): these figures are given in Table 8. From these results a plot of log $[(dn_g/dt)_{t=0}]$ yields an apparent activation energy of about 13·8 kcal. mole^{-1}. It is seen that in this pressure range the rate is roughly proportional to pressure (cf. expts. A3 and A12, and A9 and A10); also from expts. A1 and A2 the surface is not covered after the adsorption of 2·0 × 10^{17} atoms/g., since at least a further 1·5 × 10^{17} atoms/g. can be readily taken up at about the same pressure, in fact at an initial rate greater than that of the first adsorption on the freshly-outgassed oxide.

It is noteworthy that the rate of bombardment of the surface of 1 g. of oxide (taken as 62 m.^{2} from the B.E.T. results of Table 6) at 456° is about 8·6 × 10^{25} molecules/min. at a pressure of 10^{-3} cm., according to simple kinetic gas theory: multiplication of this by the factor $\exp(-13{,}800/\boldsymbol{RT})$ gives approximately 1·25 × 10^{21} atoms per g. per min., which is roughly 10^5 times the observed rate of adsorption at this temperature.

It was established that the rate of desorption from a partly-covered surface was slow. For instance, after the adsorption on 20 g. of oxide at 6 cm. pressure at 485°, the furnace temperature was raised to 540°, and the oxide evacuated for 15 min.; at the end of this time the pressure during pumping was 4 × 10^{-3} mm., and when the pumps were cut off the pressure rise in the adsorption system during 3 min. corresponded to a desorption rate of 3·4 × 10^{15} atoms per g. per min. After a further 2 hours' pumping the corresponding figures were 6 × 10^{-4} mm. and 5·4 × 10^{14} atoms per g. per min.

Discussion

(*a*) *Adsorption Studies.*—It is interesting to compare the rates of exchange (at ~6 cm.) with those of adsorption (at ~10^{-3} cm.) at temperatures 456° and 388°, which fall respectively in the regions of low and high activation energy for the exchange reaction. The initial rate of exchange, v_0, atoms per g. per min., may readily be shown to be given by

$$v_0 = n_g/w\ (-d\alpha/dt)_{t=0} = n_g k_e/w\ (\alpha_0 - \alpha_\infty)$$

where k_e is the experimental first-order rate constant, $n_g/2$ is the number of oxygen molecules in the gas phase, and α_0 and α_∞ are the ^{18}O abundances of the gas respectively

at the beginning and the end of the reaction. The initial rate of adsorption, $v_a = -(dn_g/dt)_{t=0}$ (cf. Table 8), and if this process is rate-determining, the maximum possible initial exchange rate would be $(\alpha_0 - \beta_0)v_a$, where β_0 is the initial ^{18}O content of the oxide. For these two temperatures, with oxide outgassed at 540°, $v_0 = 1{\cdot}1 \times 10^{17}$, $(\alpha_0 - \beta_0)v_a = 1{\cdot}1 \times 10^{14}$ (456°), and $v_0 = 2{\cdot}6 \times 10^{16}$, $(\alpha_0 - \beta_0)v_a = 5{\cdot}6 \times 10^{13}$ (388°) atoms per g. per min. Since adsorption must precede exchange, we conclude that measurements of initial adsorption rates at low pressures on to an outgassed surface can tell us little about the rate-limiting factors in the exchange process at several cm. pressure. It may be remarked that at 388°, where adsorption (at 6 cm.) appeared complete in <5 min., the exchange, similar proportions of oxide and oxygen being used, had a time of half-change of 62 min.; the corresponding figures for 456° were <10 and 17·3 min. However, the accuracy of these adsorption-rate measurements was low. It is unfortunately not possible to measure adsorption rates over a range of pressures from 10^{-3} to 6 cm. so as to determine the pressure dependence of the process, but assuming $v_a \propto p_{O_2}$ the values of $(\alpha_0 - \beta_0)v_a$ become $3{\cdot}4 \times 10^{17}$ (388°) and $6{\cdot}6 \times 10^{17}$ (456°), which are both greater than the corresponding v_0 figures.

It must be noted that the validity of a comparison of these figures with the values of v_0 given above is doubtful since, apart from the long extrapolation involved in assuming $v_a \propto p_{O_2}$, the oxide surface is undoubtedly heterogeneous, as shown by the change of n_s with temperature (cf. Table 4 and Fig. 1), and indicated also by the very low coverage (~0·1% of the exchangeable surface, which is itself roughly equal to the B.E.T. area) at 6 cm. It is probably best to conclude that the adsorption studies do not allow us to reject either adsorption or desorption as possible rate-determining steps in the exchange process, although it is probable that adsorption is not the slow stage.

(*b*) *Exchange Reaction.*—Some discussion has been given elsewhere of the kinetics of this process (Houghton, Thesis, London, 1952; Houghton and Winter, *op. cit.*; Winter, *loc. cit.*), but some recapitulation and extension is convenient here, the notation of an earlier paper (Winter, *Discuss. Faraday Soc.*, 1950, **8**, 231) being used.

We may generalise the approach used there by assuming that the velocity of exchange, v atoms min.$^{-1}$, will be proportional to the product of a function $f(C_g)$ of the surface coverage with oxygen, and a function $\phi(n_s)$ of the exchangeable surface. Then

$$v = -n_g(d\alpha/dt) = k_e n_g (\alpha - \alpha_\infty) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$= wk_1 f(C_g)\phi(n_s) (\alpha - \beta) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and remembering that the ^{18}O content of the reaction system remains constant,

$$(\alpha_0 - \alpha_\infty)n_g = wn_s (\alpha_\infty - \beta_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

we have finally

$$k_0 n_s = k_1 f(C_g)\phi(n_s) = n_s k_e [(\alpha_\infty - \beta_0)/(\alpha_0 - \beta_0)] \quad . \quad . \quad . \quad . \quad (8)$$

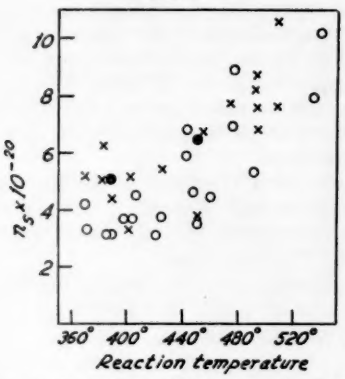
which may be compared with eqns. (2)—(11) of the paper given above.

It is thus seen that $k_0 n_s$ may be a more important function than k_0; only when the term $f(C_g)\phi(n_s)$ contains n_s as a simple factor will it be correct to use k_0: a brief discussion of some possible cases when the use of k_0 is justified has been given elsewhere (Winter, *loc. cit.*); a more detailed argument has been developed by Houghton (Thesis, London, 1952). In any case it must be remembered that neither k_0 nor $k_0 n_s$ is likely to be identical with the true rate constant k_1, and activation energies calculated from the variation with temperature of these two functions will include the effect of temperature upon $f(C_g)$ and $\phi(n_s)$.

Possible rate-determining processes in the exchange are (*a*) adsorption of oxygen molecules, (*b*) dissociation of adsorbed molecules to ad-atoms, (*c*) diffusion of adsorbed atoms or molecules over the oxide surface, into surface cracks, pores, etc., (*d*) exchange proper, which must involve electron transfer between adsorbed oxygen and lattice oxygen or suitable lattice defects, (*e*) recombination of ad-atoms to molecules, (*f*) desorption of oxygen molecules, and (*g*) gaseous diffusion through the powdered oxide. Now processes (*a*) and (*f*) involve only van der Waals forces; it has been established (Winter, unpublished work) that at liquid-oxygen temperatures *physical* adsorption and desorption of oxygen on

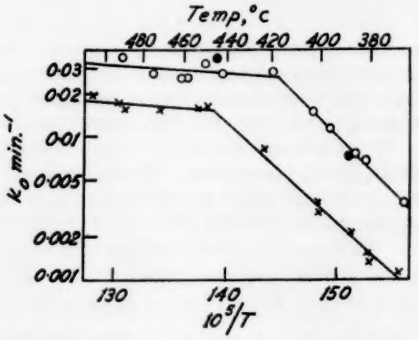
the magnesium oxide used in this study are rapid, being complete in less than a minute at oxygen pressures of 2—30 cm. We can, therefore, eliminate these as possible rate-determining steps at the much higher temperatures of the exchange reaction. We discard process (*g*) because exchange reactions in which the oxide was packed moderately firmly into a platinum boat gave the same rate constants as runs wherein the oxide was loosely spread over the bottom of the reaction vessel: this was confirmed for both slow and fast exchange rates. In addition, if (*g*) were rate-determining, the temperature dependence of k_0 (or $k_0 n_s$) should be that of the gaseous self-diffusion coefficient, *i.e.*, proportional to T^n, where $0{\cdot}5 < n < 1$; as noted above, the rate constants show an exponential dependence upon T^{-1}. A plot of log k_0 or log $k_0 n_s$ against log T in the region of low E gave a curve, from which it was obvious that $n \gg 1$. It is not possible to reject (*c*), particularly since, as we have already noted, the coverage at 6 cm. pressure is quite sparse. No unambiguous evidence upon this point was obtainable from the measurements of rates of adsorption of oxygen. It is, however, unlikely that the process of high activation energy is one of surface diffusion, although it is possible the high-temperature reaction, of low E,

FIG. 1.



× Outgassed at 510° c; p_{O_2} = 6—8 cm.
○ Outgassed at 540° c; p_{O_2} = 6—8 cm.
● Outgassed at 540° c; p_{O_2} = 1·1 cm.

FIG. 2.



× Outgassed at 510° c; p_{O_2} = 6—8 cm.
○ Outgassed at 540° c; p_{O_2} = 6—8 cm.
● Outgassed at 540° c; p_{O_2} = 1·1 cm.

is diffusion-controlled (cf. Tompkins, *Trans. Faraday Soc.*, 1950, **46**, 569; Patterson, *ibid.*, 1953, **49**, 802). Pending the completion of work now in progress, we postpone discussion of (*c*), and are left with (*b*), (*d*), and (*e*):

$$O_2(\text{ads.}) \underset{(e)}{\overset{(b)}{\rightleftharpoons}} 2O(\text{ads.}) \underset{(d)}{\overset{(d)}{\rightleftharpoons}} \text{surface exchange}$$

The experimental work presented here does not allow us to choose between (*b–e*) and (*d*) as rate-determining steps. If we assume, as seems reasonable, a rapid attainment of the steady state among the adsorbed species, reactions (*b*) and (*e*) become indistinguishable, and the apparent activation energy of the exchange reaction, when this is controlled by (*b*)(*e*), will, in the usual way, reflect the change with temperature of the equilibrium between O_2(ads.) and O(ads.). Thus, considering this case, if we assume the rate of dissociation is proportional to the stationary concentration of O_2(ads.) and that the equilibrium lies well to the right (as is very probable since the lifetime of O_2 on the surface at these temperatures is likely to be much less than that of an oxygen atom), then

$$k_{(b)} C_g \gamma = k_{(e)} C_g^2 (1 - \gamma)^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where C_g is the total concentration of adsorbed oxygen (atoms and molecules) expressed as atoms/g. of oxide, and $k_{(b)}$, $k_{(e)}$, are the corresponding rate constants. We have already assumed $k_{(b)} \gg k_{(e)}$, so that the degree of association, γ, of the oxygen is small, and

$$k_{(b)} C_g \gamma \approx k_{(e)} C_g^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Then it follows from eqn. (8) that

$$k_{(e)}C_g^2 = n_s k_0 = n_s k_e [(\alpha_\infty - \beta_0)/(\alpha_0 - \beta_0)] \quad . \quad . \quad . \quad . \quad (11)$$

where k_e is the experimental first-order rate constant of the exchange reaction. If we further assume $C_g \propto n_s$, then (11) reduces to

$$k_{(e)}'C_g = k_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

For the case when (*d*) is rate-determining, we have the result (Winter, *loc. cit.*)

$$k_{(d)}C_g = k_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

Note that in the derivation of eqn. (13) no assumption is needed regarding the relation between C_g and n_s.

We may note also that the exchangeable oxygen, n_s, in the oxide surface (in atoms/g. of oxide), is given by eqn. (7), thus

$$n_s = (n_g/w)\ (\alpha_0 - \alpha_\infty)/(\alpha_\infty - \beta_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

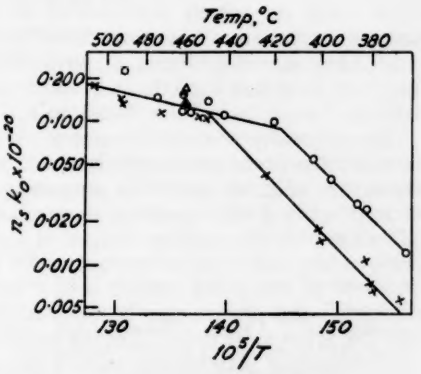


FIG. 3. ×, ○, △, ▲, ◓: Outgassed at 510°, 540°, 600°, 640°, and 748° C, respectively.

The experimental figures are presented in Fig. 2 in terms of k_0, and in accordance with the above analysis there is clear evidence of two processes, the characteristics of which are shown in Table 5.

It may be noted that if (*b*)–(*e*) is rate-determining and C_g is not proportional to n_s, then log $k_0 n_s$ and not log k_0 should be used in the Arrhenius plot; if this is done with the data of Table 4, Fig. 3 results, in which the distinction between the two outgassing temperatures disappears for the high-temperature process and its activation energy is now $7{\cdot}7 \pm 2$ kcal. mole^{-1}; the activation energy for the lower-temperature region is not much changed, being $37{\cdot}6 \pm 2$ and $35{\cdot}9 \pm 1$ kcal. mole^{-1} for outgassing temperatures of 510° and 540°, respectively.

There are a number of other interesting points arising from the above kinetic analysis: thus the rate constants are not very dependent upon the oxygen pressure (Table 3), which may mean that in spite of the sparse coverage of the surface, the active sites are effectively saturated at pressures of 1 cm. upwards; *i.e.*, that C_g is virtually independent of p_{O_2} above 1 cm. up to the highest pressure used, *viz.*, 14·7 cm.

The figures recorded in Table 7 were obtained before the importance of standardising the outgassing temperature was realised; they indicate an apparent activation energy for k_0 of about 26·5 kcal./mole^{-1}. These experiments refer to temperatures at which the " true " activation energy, at constant outgassing temperature, is around 3 kcal. mole^{-1} (cf. Table 4 and Figs. 1 and 3); it is likely that the difference reflects mainly an increase in the number (S_c) of reactive sites as the outgassing temperature is raised, thus we may write

$$k_0 = A \exp(-E/RT) = S_c Z_c \exp(-E/RT)$$

where A is the coefficient of intrinsic catalytic activity (cf. Schwab, *Z. physikal. Chem.*, 1929, **5**, *B*, 406; 1930, **9**, *B*, 265; *Trans. Faraday Soc.*, 1946, **42**, 689; Balandin, *Z. physikal. Chem.*, 1932, **19**, *B*, 451; Eckell, *Z. Elektrochem.*, 1933, **39**, 859; Cremer, *Z. physikal. Chem.*, 1929, **144**, *A*, 231; Storch, *J. Amer. Chem. Soc.*, 1935, **57**, 1395; Huttig, *Kolloid-Z.*, 1941, **98**, 263, and papers there cited), Z_e is the frequency factor for energy transfer between the reactant species, and S_e is the number of active sites on the catalyst surface. If this type of behaviour is typical, it indicates the great difficulty of properly interpreting heterogeneous catalytic phenomena. It is unfortunate in this connection that the figures given in Table 5 and eqns. (1)—(4) are not sufficiently accurate to show whether the increase in rate with outgassing temperature at constant reaction temperature is due to a change in A or in E. The values for k_0 at ~460° on samples outgassed at temperatures from 866° to 510° yield the Arrhenius equation $k_0 = 19{\cdot}1 \exp(-10{,}900 \pm 700/\boldsymbol{RT})$, if it is assumed that k_0 properly refers to the high-temperature exchange reaction. Alternatively, if $k_0 n_s$ should be used, it is seen from the last column of Table 2 that the product rises to a flat maximum between outgassing temperatures of 550° and 750°, falling sharply at 866°. This is very similar to the effect found by Huttig (*Z. physikal. Chem.*, 1934, **171**, 83; *Z. anorg. Chem.*, 1935, **223**, 241; *Kolloid-Z.*, 1942, **98**, 6, 263) for the decomposition of nitrous oxide on spinels heat-treated at various temperatures. The sharp drop in reactivity, expressed as $k_0 n_s$, around 750° (~0·33 T_m) is in agreement with the conclusions (Bevan, Shelton, and Anderson, *J.*, 1948, 1728) that surface defects become mobile between 0·3 and 0·5 T_m, where T_m is the m. p. of the solid: the commencement of sintering is shown clearly by the results in Table 2 and the B.E.T. figures in Table 9.

The complexity of even the present, at first sight simple, reaction is further demonstrated by the heterogeneity of the oxide surface—as in the change of n_s with reaction temperature (Fig. 2) and with outgassing temperature (Table 2). The heterogeneity indicated in Fig. 2 may also be demonstrated and confirmed by allowing a sample to reach equilibrium with ^{18}O-enriched oxygen at a relatively low temperature, say 380°, and then quickly raising the furnace temperature by some 30°, whereupon a rapid exchange occurs with more of the oxide surface and a new equilibrium ^{18}O-content of the oxygen is established; this process may be repeated several times, but up to a reaction temperature of 507°, n_s is not more than 7% of the total oxygen in the oxide.

A comparison between the surface areas obtained from the B.E.T. plots and the n_s values obtained by exchange has been made by assuming that the surface of the magnesium oxide powder consists of a random distribution of the (111), (110), and (100) planes, then, a radius of 1·4 Å being used for the oxygen ion, the average area occupied by an oxygen ion is 10·1 Å^2, and the surface area of the oxide is given in each case by $10{\cdot}1 n_s \times 10^{-20}$ m.^{2}/g. Table 9 gives some typical results and shows that the two methods give comparable figures at outgassing temperatures of up to 640°, but diverge somewhat above this, until at 860°, when considerable sintering has occurred, the B.E.T. values are some 5—8 times those obtained from the exchange.

We are indebted to Dr. K. J. Hill and Miss D. A. Symes for the determination of a number of B.E.T. isotherms. The greater part of the ^{18}O exchange work was performed in the Department of Inorganic and Physical Chemistry, Imperial College, during 1950: we thank Professor H. V. A. Briscoe for his interest and encouragement. Acknowledgment is also made to the Central Research Fund of London University, and to the D.S.I.R. for a maintenance grant for one of us (G. H.).

1, Wheeleys Road, Birmingham, 15.
Department of Technical Chemistry,
Royal Technical College, Glasgow.

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Exchange Reactions of Solid Oxides. Part IV. Zinc Oxide.*

By J. A. Barnard, E. R. S. Winter, and H. V. A. Briscoe.

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The exchange of ^{18}O between the surface of zinc oxide and oxygen gas has been studied over the temperature range 367—630°, with oxygen pressures from 1 to 25 cm. The rate of exchange and the amount of exchangeable oxide surface depend on the previous outgassing of the oxide. The exchange rates are dependent upon $(p_{O_2})^{1\cdot0 \pm 0\cdot1}$ over the whole temperature range and have $E = 0\cdot5 \pm 1$ kcal. mole^{-1} at high temperatures and $27\cdot5 \pm 1\cdot0$ kcal. mole^{-1} at lower: the change of mechanism occurs at 510° for oxide outgassed at 580°, and at 415° for oxide outgassed at 630°. It is not possible to identify with certainty the rate-determining step in the exchange, but it is probable that the exchange reaction proper has $E = 27\cdot5$ kcal. mole^{-1} and that the other figure refers to surface migration of adsorbed oxygen. Semi-conductivity measurements on this preparation of zinc oxide gave $E = 27\cdot5$ kcal. mole^{-1} at $p_{O_2} = 60$ mm.

As an extension of earlier work (*J.*, 1950, 1170, 1175, and Part III *) we have studied the exchange of ^{18}O between zinc oxide and ^{18}O-enriched oxygen gas. Zinc oxide was chosen since more is known about its semi-conductivity properties than is the case with the other oxides so far examined. The exchange kinetics are formally similar to those found for magnesium oxide (Part III), except that the rate increases markedly with increase of oxygen pressure; in an effort to elucidate the mechanism of the exchange, measurements were undertaken of the adsorption of oxygen on zinc oxide and of the semiconductivity of the oxide. The symbols used in this paper have the same significance as in Part III.

Experimental

Materials.—The enriched oxygen, containing some 1·2% excess of ^{18}O, was prepared as before (Part III). Normal oxygen was obtained by heating "AnalaR" potassium permanganate. Spectroscopically pure neon was from the British Oxygen Co. Nitrogen for the B.E.T. measurements was taken from a cylinder and passed through concentrated sulphuric acid, over heated copper, and finally through a trap at −78° into the adsorption apparatus. The zinc oxide was made by burning 99·99% zinc in air.

Exchange Experiments.—The experimental method has been described in Part I (*J.*, 1950, 1170); samples of about 3 g. of oxide with about 5 ml. (N.T.P.) of oxygen gave reasonable changes in ^{18}O content. The technique was improved by using an electronic device to control the furnace temperature and by recording the temperature at 30-sec. intervals throughout most runs, including the outgassing period, with a Cambridge thread recorder so operated as to be sensitive to changes of <0·5°. The controller, working off a platinum-resistance thermometer wound on the furnace tube, kept the temperature constant to with ±0·5° overnight.

Adsorption Measurements.—B.E.T. isotherms were obtained in the usual manner, nitrogen being used as the adsorbate, at 78° K: the oxide was first outgassed overnight at temperatures from 150° to 630°.

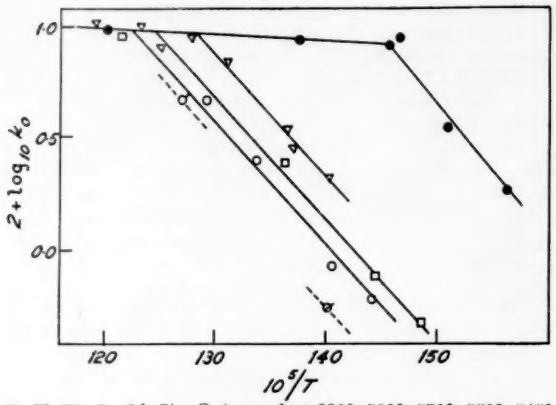
Oxygen-adsorption measurements were carried out in a constant-volume apparatus of conventional design. Pressures from 10^{-3} to 15 mm. were measured by McLeod gauge: at the upper end of this range a correction was applied for the pressure exerted by the system on the open limb of the gauge. Pressures above 15 mm. were read on a wide-bore U-tube manometer with the aid of a cathetometer. Oxide samples (30 g.) were subjected to the same pretreatment, by outgassing for 16 hr. at a steady elevated temperature, as was used in the exchange experiments: if the limiting pressure reached during the outgassing was $>10^{-5}$ mm. the run was discarded. After completion of the oxygen adsorption, the system was re-evacuated, and the volume calibration performed at the same temperature, neon being used.

Conductivity Determinations.—Pellets of oxide were prepared by compression (5 ton in.$^{-2}$), and measurements made in the cell described by Jacobs (*J. Sci. Inst.*, 1953, **30**, 204), a microammeter and a known potential source being used: standard resistances were used to check the accuracy of the figures obtained. The pellet was placed in the cell, which was then sealed

* Part III, preceding paper.

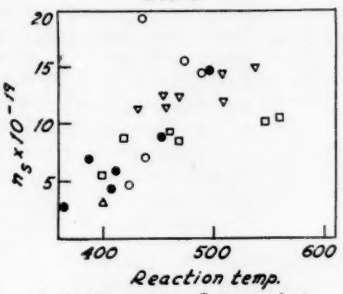
to the vacuum-line and evacuated overnight at 560°, precautions being taken to ensure that the zinc which distilled out from the pellet did not short-circuit the cell. During outgassing the resistance fell from several megohms to ~80Ω. Oxygen was admitted until the pressure was 60 mm., whereupon the resistance rose very rapidly to several megohms and became steady. The temperature was lowered, and the resistance altered as rapidly as the temperature to the

FIG. 1.



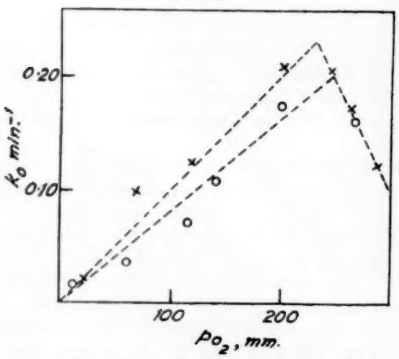
●, ▽, □, ○, ◐, ◌: Outgassed at 630°, 580°, 570°, 550°, 545°, and 530°, respectively.

FIG. 2.



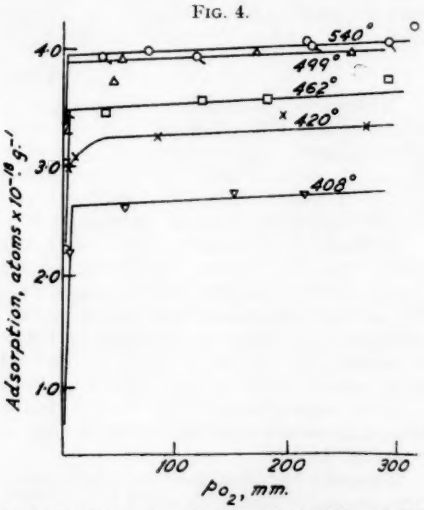
△, ●, ▽, □, ○: Outgassed at 698°, 630°, 580°, 570°, and 550°, respectively.

FIG. 3.



× : Outgassed at 630°; reaction at 560°.
○ : Outgassed at 570°; reaction at 474°.

FIG. 4.



○, ◌, □, ▽; △, ×: Outgassed at 560° and 522°, respectively.

new equilibrium value; in this way the resistance of the pellet was measured over the range 560—450°.

Results.—Oxygen exchange. Values of k_0 and n_s were obtained as previously described; the kinetic runs gave good first-order plots. It is seen from Figs. 1 and 2 that for zinc oxide the variations of k_0 and n_s with both reaction and outgassing temperature are very similar to the behaviour of magnesium oxide; if anything, zinc oxide is more sensitive to outgassing conditions than the latter oxide, but this is masked in the present results because of the closer temperature control exerted here. However, a plot of $\log k_0 n_s$ against $10^5/T$ shows considerably more scatter than Fig. 3 of Part III, although showing the same general characteristics. Activation energies from Fig. 1 are 0·5 ± 1 kcal. mole^{-1} for the high-temperature region, and

27·5 ± 1 kcal. mole^{-1} for the lower temperatures. Fig. 3 shows that k_0 depends strongly upon the pressure of oxygen used; for this reason the experiments of Fig. 1 were done at pressures between 50 and 75 mm. A few results at lower pressures (~10 mm.) showed that n_s has no systematic variation with pressure. A plot of log k_0 against log p_{O_2} from Fig. 3 was made and showed that $k_0 \propto (p_{O_2})^{1\cdot0 \pm 0\cdot1}$ up to the point of inflexion which occurs for both temperatures at about 220 mm. The fall of k_0 at higher pressures is believed to be because the rate of diffusion through the leak into the mass spectrometer was becoming the slow stage; this would explain why the fall takes place at about the same p_{O_2} and k_0 at two different reaction temperatures. An alternative explanation may be that the inflexion points represent the onset of changes in the adsorbed state; *i.e.*, changes in C_g, completion of one layer of adsorbed oxygen, etc., but this is most unlikely to be occurring at the same pressure at two widely different temperatures, where the activation energies of the exchange reaction are so different. Some experiments illustrating the importance of standardising the time of outgassing are summarised in Table 1, and the results of a few poisoning experiments are given in Table 2; the effect of incomplete outgassing (time or pressure) is significant, and all experiments with the exception of these were conducted under a strict routine of outgassing for 16 hr. to a pressure $<10^{-5}$ mm.: if the pressure at the end of 16 hr. was too high the run was discarded. It will be recalled that magnesium oxide shows a similar sensitivity to pretreatment (Part III, *loc. cit.*), but that, whereas k_0 for the latter increases with increasing outgassing time, yet in the case of zinc oxide a decrease is observed. Like magnesium oxide, our specimen of zinc oxide shows clear evidence of heterogeneity (cf. Fig. 2).

TABLE 1. *Effect of time of outgassing on rate of exhange.*

Temp. of outgassing	Time (hr.)	Run temp.	k_0, min.$^{-1}$	$10^{-20}n_s$, atoms g.$^{-1}$	Temp. of outgassing	Time (hr.)	Run temp.	k_0, min.$^{-1}$	$10^{-20}n_s$, atoms g.$^{-1}$
(a) *Low-temperature region*					(b) *High-temperature region*				
580°	4	457°	(not 1st order)	0·91	570°	4	540°	0·127	1·37
580	16	457	0·0336	1·16	570	4½	540	0·139	1·04
580	60	457	0·0294	1·27	570	16	540	0·0927	1·20

TABLE 2. *Poisoning experiments.*

Expt. No.	Outgassing temp.	Run temp.	k_0, min.$^{-1}$	k_0, min.$^{-1}$ (Interpolated from Fig. 1)
Heated with benzene				
1	565°	470°	0·0571	0·0368
Heated with water				
2	565	478	0·0695	0·0394
Heated in 10^{-2} mm. of air overnight				
3	630	560	0·650	0·0927
4	630	398	0·0840	0·0476
5	630 *	475	0·0682	0·090
6	630 *	387	0·00494	0·036

* In these two experiments the oxide, after outgassing, was treated with 6 cm. of O_2 for *ca.* 7 hr. and then re-evacuated at 630° overnight before the rate of exchange was measured.

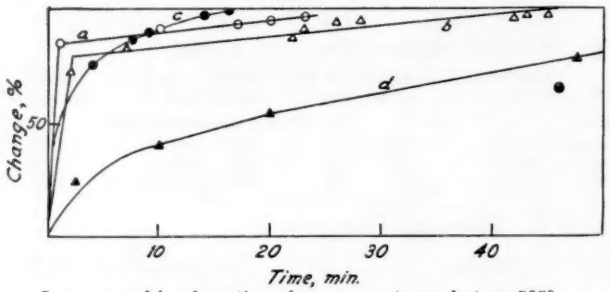
Adsorption measurements. (*a*) B.E.T. Samples of zinc oxide outgassed overnight at 570° and at 630° gave B.E.T. areas of 5·30 and 5·25 m.^{2} g.$^{-1}$, respectively; a sample outgassed overnight at 150° gave an area of 6·35 m.^{2} g.$^{-1}$. Good B.E.T. plots were obtained; an area of 16·2 Å^2 was assumed for the nitrogen molecule (cf. Part III, *loc. cit.*).

(*b*) *Oxygen-adsorption experiments.* The adsorption isotherms are given in Fig. 4: the amount of gas taken up at equilibrium is independent of outgassing temperature and substantially independent of pressure above ~25 mm.; this uptake is rapid at all temperatures studied, 70% or more being complete in no more than 2 min., and once equilibrium is reached, usually in less than an hour, no further change occurs even after 72 hr. The adsorption is irreversible since after 16 hr.' pumping at 460° of a sample which at this temperature had reached adsorption equilibrium with 310 mm. oxygen, no further uptake is detectable at 337 mm. oxygen pressure: this experiment would have detected an adsorption of 2×10^{17} atoms g.$^{-1}$, which corresponds to about 0·5% of the B.E.T. surface. However, if the temperature of the sample is raised, oxygen is taken up until the higher-temperature isotherm is reached: the reverse process does not occur. It appears clear that at any rate the greater part of the adsorption is chemisorption, probably mainly on to metallic zinc exposed during the

outgassing treatment. In this connection it is noteworthy that the oxide used contained significant amounts of unoxidised metal; this was not apparent on microscopic examination but at the end of each outgassing treatment a zinc mirror had distilled on to cool portions of the reaction tube just outside the furnace: it is probable, particularly in view of the method of preparation, that many of the oxide particles contained small cores of metal. Since the amount of chemisorption often increases at lower temperatures, adsorption on an oxygenated surface was sought at 260° and at 200° but none was found; the oxide was here pumped overnight at 550° and treated with 89 mm. of oxygen at that temperature until adsorption was complete, pumped hard, and cooled to 200° (or 260°), whereat further oxygen was added; no adsorption (to $\pm 2 \times 10^{17}$ atoms g.$^{-1}$) was detectable up to 257 mm.

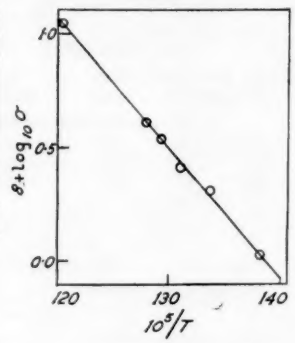
The rate of adsorption was followed by taking pressure measurements at intervals during the uptake of the first dose of oxygen; in these experiments the initial pressure was about 10 mm., falling to between 0·5 and 5·0 mm. at equilibrium. On examining the results it was at once apparent that the initial very rapid adsorption was a different process from the slow disappearance of the last 10—20%. Attempts to separate the two processes, by assuming various mechanisms and adopting different methods of extrapolation to zero time, were not successful, the resulting rate constants showing considerable scatter. We therefore shall not consider the results in detail here; two typical experiments are shown in Fig. 5, together with two exchange-reaction curves determined under similar experimental conditions.

FIG. 5.



Curves *a* and *b*, adsorption of oxygen, outgassed at *ca.* 565°.
Curves *c* and *d*, exchange of oxygen, outgassed at 570°
Reaction temperatures: *a*, 540°; *b*, 462°; *c*, 550°; *d*, 461°.

FIG. 6.



Conductivity determinations. The results are shown in Fig. 6, and fit an equation of the form $\sigma = A \exp(-E/RT)$, where σ is the conductivity, $A = 2{\cdot}00$ mhos, and $E = 27{\cdot}5$ kcal. mole^{-1}. Recorded values for E for this oxide vary widely, but the recent work of Hogarth (*Z. physikal. Chem.*, 1951, *A*, **198**, 30) gives a value of 26·4 kcal. mole^{-1} in the temperature range 560—640°, at a p_{O_2} of *ca.* 50 mm.

DISCUSSION

When we try to decide, from the work reported here, the exact nature of the rate-determining steps in the exchange reaction we are faced with a very similar situation to that found with magnesium oxide (preceding paper). Thus, by the same arguments we are left with processes (*b*), (*c*), (*d*), and (*e*) of that paper as possible rate-determining steps. With regard to (*c*)—migration of oxygen over the surface from the adsorption or desorption sites to exchange sites—we note that the n_s values from the exchange work are of the order of 10^{20} atoms g.$^{-1}$, and assuming a surface of oxygen ions the B.E.T. figures give a value of about 6×10^{19} atoms g.$^{-1}$; the total oxygen adsorption is about 3—4×10^{18} atoms g.$^{-1}$ at comparable temperatures to those used in the exchange studies, and this value undoubtedly includes a large contribution due to oxidation of metallic zinc. It appears that the coverage with oxygen is sufficiently sparse for surface migration to remain a possible rate-determining step.

In considering the surface exchange reaction [(*d*) of Part III] as possibly rate-determining, the fact that the apparent activation energy of the low-temperature exchange reaction is the same as that found for the conductivity might be thought significant. It could be postulated that the exchange sites are identical with (or at least closely connected

with, in position and number) the semiconductivity sites in the surface, which for zinc oxide are almost certainly interstitial zinc atoms, Zn_i (von Baumbach and Wagner, *Z. physikal. Chem.*, **1933**, *B*, **22**, 199; Bevan and Anderson, *Discuss. Faraday Soc.*, **1950**, **8**, 239). The exchange reaction could then be written

$$Zn_i^{2+} + O_i^{2-} \rightleftharpoons O_{ads.} + Zn_i$$

$O_{ads.}$ representing chemisorbed oxygen in isotopic equilibrium with the gas phase. The continuous formation and destruction of Zn_i at various points in or just beneath the surface would then account for the exchange's slowly spreading over the whole surface. This is an attractive hypothesis and may well be close to the truth, but in certain important respects it does not account for our observations. It has been shown (*idem, locc. cit.*) that the above equation accounts satisfactorily for the observed dependence of the semiconductivity, σ, upon oxygen pressure, p_{O_2}, at pressures above about 10^{-3} cm., thus $\sigma \propto p_{O_2}^{-\frac{1}{4}}$, while $[Zn_i] \propto p_{O_2}^{-\frac{1}{6}}$, so that if we write the exchange rate as $\propto [Zn_i][O_{ads.}]$ it should be independent of p_{O_2}: our results (Fig. 3) show that $k_0 \propto (p_{O_2})^{1\cdot0\pm0\cdot1}$ (although, in fact, we have not directly demonstrated that the exchange mechanism is the same at any one temperature, over the whole pressure range studied). Since the exchange reaction on magnesium oxide, which exhibits no semiconductivity properties at these temperatures, occurs roughly as readily as on the semiconducting zinc oxide we incline to the view that there is no direct relation between exchange and conductivity, and conclude that the agreement between the two activation energies in the case of zinc oxide is probably fortuitous.

As in the case of magnesium oxide, we tentatively ascribe the exchange reaction of high E (27·5 kcal. mole^{-1}) to the true exchange reaction, and that with $E = 0\cdot5 \pm 1\cdot0$ kcal. mole^{-1} to the migration of ad-atoms of oxygen over the oxide surface. Evidence in support of this assignment of mechanisms is given in Part V (following paper).

The experiments detailed in Table 2 are interesting, but little definite information regarding mechanisms can be drawn from them. It is seen that exposure to a high pressure of oxygen at 630° before exchange (Expts. 5 and 6) affects the reaction of low E hardly at all, but decreases that of high E very considerably; exposure to very low oxygen pressure increases the speed of both reactions. These observations are doubtless connected with the likelihood that (*a*) exposure to the lower oxygen pressure will lead to much less adsorption–desorption and exchange of oxygen, so that it is likely that less sintering occurs under these conditions—this could well lead to a more active surface—(*b*) the lower oxygen pressure would leave a higher concentration of Zn_i in and near the surface, and this may well increase the speed of any exchange process involving reaction of $O_{ads.}$ with Zn_i. It is known from the work of Bevan and Anderson (*loc. cit.*) that surface defects are largely frozen in the surface of zinc oxide below about $0\cdot3T_m$ ($\approx$900°); if the rate of the exchange reaction of $E = 27\cdot5$ kcal. mole^{-1} is proportional to $[Zn_i]$ we would expect it to be increased by increasing the outgassing temperature (*in vacuo*) (provided the temperature was not too near 900°, so that no sintering occurred). This is in fact observed (cf. Fig. 1), the temperature at which change occurs to a high-temperature reaction of low E being 510° when outgassed at 580°, and 415° when outgassed at 630°; similar observations were, however, made on magnesium oxide (cf. Part III, *loc. cit.*) in which the presence of Mg_i has not been demonstrated so far as we know.

This work was facilitated by financial assistance from the Central Research Fund of London University and the D.S.I.R., whom we thank. One of us (J. A. B.) also acknowledges a maintenance grant from the D.S.I.R. We are indebted to Mr. Fishwick, of Fricker's Metal Co., for kindly preparing the zinc oxide, and to Dr. P. W. M. Jacobs for advice on the semiconductivity measurements.

1, Wheeleys Road, Birmingham, 15.

Department of Inorganic and Physical Chemistry,
Imperial College, London, S.W.7.

[Present address (J. A. B.): Dept. of Chemical Engineering,
University College, London, W.C.1.]

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Exchange Reactions of Solid Oxides. Part V. Dissociation of Molecular Oxygen at Oxide Surfaces: Magnesium Oxide and Zinc Oxide.*

By E. R. S. Winter.

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The reaction $^{18}O_2 + {}^{16}O_2 \rightleftharpoons 2{}^{16}O{}^{18}O$, taking place on the surface of zinc oxide and magnesium oxide, has been studied at temperatures such that oxygen exchange with the surface did not occur. For magnesium oxide the equilibration reaction has $E = 6{\cdot}5 \pm 0{\cdot}5$ kcal. mole^{-1}, and varies as $(p_{O_2})^{1{\cdot}0}$; it is much faster than the oxygen-exchange reaction and it is concluded that adsorption–desorption cannot be rate-determining steps in the latter. For zinc oxide the equilibration reaction has $E = 22 \pm 1{\cdot}0$ kcal. mole^{-1} below 215° and $8{\cdot}5 \pm 1{\cdot}0$ kcal. mole^{-1} above this; the rate varies as $(p_{O_2})^{1{\cdot}0}$ throughout. By comparison with earlier observations upon oxygen adsorption and exchange it is concluded that the latter figure for E refers to migration of oxygen atoms over the oxide surface, and the former to the adsorption and desorption of oxygen.

The earlier papers in this series (*J.*, 1950, 1170, 1175; Parts III and IV *; see also *Discuss. Faraday Soc.*, 1950, **8**, 231; *Nature*, 1949, **164**, 1130) have been concerned with the kinetics of ^{18}O exchange between gaseous oxygen and the surface layer of oxygen ions of various oxides. The oxides fully examined, *viz.*, Cr_2O_3, MgO, and ZnO, exhibit the same general phenomena: there is one exchange reaction at high temperatures (above about 400—450°) with a low apparent activation energy (0—8 kcal. mole^{-1}) and another at lower temperatures with an apparent activation energy of 25—40 kcal. mole^{-1}. Owing to the difficulty of measuring the rates of adsorption and desorption, and in two cases the small amount of adsorption, at pressures similar to those used in the exchange experiments (Cr_2O_3 will be considered in more detail in another paper), it has not been possible to determine the nature of the rate-determining steps in the exchange reactions, although tentative identifications have been made. The exchange step involves dissociation of the oxygen molecule, either at the moment of exchange or earlier, during the adsorption stage; no direct measurements of this process have been attempted hitherto. The work now reported consists essentially of studies on the rate of equilibration of a mixture of $^{16}O_2$ and $^{18}O_2$ molecules, exposed to samples of the oxides used in the exchange work: $^{16}O_2 + {}^{18}O_2 \rightleftharpoons 2{}^{16}O{}^{18}O$; the temperatures used were such that isotopic exchange with the oxide surface did not occur.

In practice, a mixture of pure $^{18}O_2$ and $^{16}O_2$ was not used; instead a 1:1 mixture of normal oxygen and a fully equilibrated sample containing *ca.* 30% of ^{18}O was exposed to the oxide, and the reaction followed by watching the approach of the 32/36 mass ratio to the equilibrated figure corresponding to *ca.* 15% of ^{18}O.

Experimental

Materials.—The oxides used were from the same well-mixed batches which were prepared for use in the exchange reactions: fresh samples were used for each experiment. Gaseous oxygen containing about 30% of ^{18}O was prepared by thermal diffusion, using a hot-wire column, from oxygen obtained by electrolysis of water containing about 12% of ^{18}O. Normal oxygen was made by heating potassium permanganate, as described in Part III (*J.*, 1954, **1509**).

The enriched oxygen prepared by thermal diffusion was shown by analysis to be in isotopic equilibrium; thus the % of ^{18}O was the same, whether calculated from the 32/34, 34/36, or 36/32 ratios: this indicated no separation of mass 34 from 36 in the column, showing that the reaction $^{18}O_2 + {}^{16}O_2 \rightleftharpoons 2{}^{18}O{}^{16}O$ occurred readily on the platinum–rhodium and nichrome wires used at temperatures near 1000° (cf. Clusius and Dickel, *Naturwiss.*, 1943, **31**, 210). A stock was prepared of oxygen consisting of a mixture of equal volumes of the normal gas and

* Parts III and IV, preceding papers.

that containing *ca.* 30% of ^{18}O: this mixture was kept in a black-painted glass bulb in case incident light caused equilibration, and no equilibration was detected at room temperature in six months. The mixture, analysed in the mass spectrometer, had a highly abnormal 32/36 ratio, as can be seen from the following figures, which refer to an approximately 1 : 1 mixture of normal and of 30·7% ^{18}O : 32/36 ratio before equilibration = 14·83, after equilibration 27·50 (Calc., 27·46). With a constant galvanometer deflection of some 15,000 cm. for mass 32 the above figures imply a fall in the mass 36 deflection from about 1000 cm. to less than 550 cm.; this fall is measurable to better than $\pm 0{\cdot}2\%$, but observations taken during kinetic runs are not likely to be correct to better than $\pm 1\%$.

Method.—The experimental procedure was exactly that used in the exchange work; a suitable weight (usually 1—3 g.) of oxide was outgassed overnight at a temperature used in the exchange work, *viz.*, 540° (MgO) and 630° (ZnO). In the morning the final vacuum was checked and if satisfactory the sample was isolated from the pumps and cooled to the desired temperature, and the requisite amount (usually *ca.* 5 ml., N.T.P.) of non-equilibrated oxygen admitted. A record of the change with time of the 32/36 (and in some cases 32/34) ratio was taken by drawing off oxygen continuously through a leak into the ion source of the mass spectrometer and following the change in 32 : 34 : 36 peak heights. The reaction system was of similar design to that used in the oxygen-exchange experiments (see Part I, *J.*, 1950, 1170); the reaction vessel used, however, was of silica. The mass spectrometer was a 60° sector Nier-type instrument, with the circuits of Graham, Harkness, and Thode (*J. Sci. Instr.*, 1947, **24**; 119), and very similar to that used in earlier work, but had an all-metal analyser tube. Ion currents corresponding to the various masses were measured by a galvanometer and shunt system; masses were brought into focus by manual voltage scanning.

A few very slow reactions were performed in a modified apparatus in which a small Töpler pump was interposed between the reaction vessel and the leak to the mass spectrometer. After suitable time intervals most of the oxygen was withdrawn from the reaction vessel and forced into a small volume attached to the leak until the pressure was high enough for accurate analysis, and after measurement the oxygen was returned to the reaction vessel. This procedure was adopted to avoid excessive loss of oxygen from the reaction system; by this means runs of several days' duration were carried out with no detectable change in oxygen pressure; the time taken to perform the measurements was negligible when compared with the total reaction time.

Kinetics.—As expected for an isotopic reaction, it was found that the fall of the 36-mass peak to the equilibrium value followed a first-order law, thus

$$-\mathrm{d}x/\mathrm{d}t = k_e' x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where x is the excess abundance of mass 36, at time t, above the equilibrium value; there was a similar rise in the mass 34 abundance but this was followed in detail in only a few runs.

We use the notation of other papers in this series, *viz.*, $n_g/2$ = no. of oxygen gas molecules introduced into the reaction system at $t = 0$; w = wt. (g.) of oxide used; $C_g/2$ = no. of molecules of oxygen adsorbed on 1 g. of oxide at equilibrium at the pressure of the reaction, p_{O_2}; n_s = no. of atoms of exchangeable oxygen in the oxide surface per g.; p_{O_2} = pressure of oxygen gas (in mm. Hg); k_A, k_M, k_E, k'' are rate constants; k_e' is the experimental rate constant for the equilibration [cf. eqn. (1)]; and k_0 is a rate constant of the exchange reaction, and is defined in earlier papers (*Discuss. Faraday Soc.*, 1950, **8**, 231; Part III, *J.*, 1954, 1509).

From (1) the rate of reaction (equilibration) in the system, in atoms min.$^{-1}$, is

$$v = -n_g(\mathrm{d}x/\mathrm{d}t) = n_g k_e' x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

which we may equate to

$$k''w\mathrm{f}'(C_g)\phi'(n_s)x$$

where k'' is the rate constant of the equilibration reaction, and $\mathrm{f}'(C_g)$ and $\phi'(n_s)$ are unknown functions of the adsorbed layer and of the oxide surface; so that

$$n_g k_e' = k''w\mathrm{f}'(C_g)\phi'(n_s) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Now a similar argument applied to the exchange reaction gave

$$k_0 n_s = k'\mathrm{f}(C_g)\phi(n_s) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

[cf. Part III, *J.*, 1954, 1509; eqn. (8)].

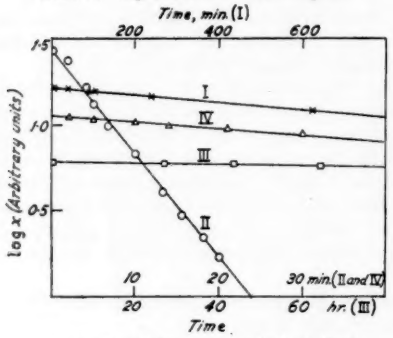
From equations (3) and (4) it follows that if the rate-determining process in the measured exchange reactions is the same as that of the equilibration reactions, then

$$k_0 n_s = n_g k_e'/w \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and since dissociation and recombination should be at least as rapid as exchange, $k_0 n_s$ should never be greater than $n_g k_e'/w$ at a given temperature. Since it is difficult to separate the exchange and equilibration reactions when both are proceeding simultaneously, the latter has been studied at temperatures low enough for the exchange reaction to be neglected, and the results extrapolated to higher temperatures by means of the Arrhenius plot (cf. Fig. 3).

Results.—The highest reaction temperature used in this work was 311°; it was first established that even at 500° the empty reaction vessel itself did not cause equilibration; thus after 40 min. at this temperature the 32/36 ratio changed by less than 1·5%, while at 100° less than 0·3% change occurred in a week: this degree of reactivity was negligible compared with that of the oxides. The inert character of the reaction vessel was again confirmed at the end of this series of experiments.

FIG. 1. *Equilibration reaction plots.*



I, MgO at 18°. II, MgO at 270°.
III, ZnO at 119°. IV, ZnO at 310°.

FIG. 2. *Dependence of reaction rate upon pressure of oxygen.*

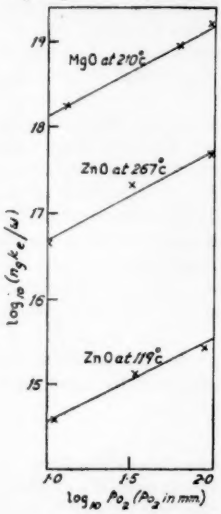


Fig. 1 shows a few plots of log x against t for the equilibration reaction on both oxides, providing experimental evidence for the use of eqn. (1). Fig. 2 shows the variation of $n_g k_e'/w$ with oxygen pressure for the two oxides; it is evident that in both cases this function is directly proportional to p_{O_2} over the pressure range 1—10 cm. It was shown in Part III (*loc. cit.*) that, for the exchange reaction with MgO, $n_s k_0$ is approximately independent of p_{O_2}, and in Part IV it was found that $n_s k_0$ varied as $(p_{O_2})^{1/9}$ for ZnO over the pressure range 1—15 or 20 cm. The exchange kinetics of Parts III and IV were determined at a pressure of oxygen of *ca.* 6 cm. and the equilibration runs for ZnO are plotted in Fig. 3*b* in the form $\log_{10}(n_g k_e'/w p_{O_2})$ against $10^5/T$, where T is the reaction temperature, and in Fig. 3*a* are plotted also $\log_{10}(n_s k_0/p_{O_2})$ against $10^5/T$ for the exchange reaction, the results used being those of the earlier paper: the results for MgO are plotted in the form $\log_{10}(n_g k_e'/w)$ and $\log_{10}(n_s k_0)$ in Fig. 3*a*, since all equilibration runs for this oxide were done at $p_{O_2} = 6$ cm. (except those of Fig. 2).

DISCUSSION

Considering first the case of MgO, it was concluded in Part III that the following three stages could be rate-determining in the exchange reaction: (1) adsorption–desorption, (2) migration of ad-atoms on the surface, and (3) exchange proper. It was also shown that it was unlikely that adsorption was a slow step although the evidence on this point was not

unequivocal; the surface coverage at the exchange temperatures was very small (*ca.* 0·1%) so that (2) could well be a slow stage. The present observations show conclusively that adsorption–desorption involving dissociation of the oxygen molecule is faster than any step we have hitherto measured in the exchange reaction. Thus the equilibration rate measured here at 275° is slightly faster than the exchange reaction at the same pressure at *ca.* 500° (see also Fig. 4). It seems reasonable to decide, in view of this evidence and the argument presented in Part III, that the " exchange reaction " at high temperatures (> *ca.* 420°) with a low activation energy is limited by process (2), while the " exchange reaction " below *ca.* 420° is the true exchange process, involving replacement of lattice oxygen by ^{18}O-enriched ad-atoms. It is not possible to determine with certainty the true activation energies of any of these processes since, as we indicated in Part III, all the experimentally determinable quantities, $n_s k_0$, $n_g k_e'/w$, etc., contain unknown functions of C_g (and probably of n_s) and the variation of C_g with temperature at these pressures (*ca.* 6 cm.) cannot be measured with sufficient accuracy. We may note, however, that the activation energy of $(n_g k_e'/w)$ under our conditions is $6{\cdot}5 \pm 0{\cdot}5$ kcal. mole^{-1}; the direct dependence of this reaction upon oxygen pressure is consistent with an adsorption–desorption process involving dissociation. It was found in Part III that the adsorption of oxygen on this oxide, as measured by the initial rate of adsorption at pressures near 10^{-3} cm., had $E = 13{\cdot}8$ kcal. mole^{-1}; this value is unlikely to hold at pressures around 6 cm., since the surface is undoubtedly heterogeneous, as shown by the variation of n_s with temperature. We have already indicated (Part III) that it is impossible in isotopic reactions of the present type to distinguish between adsorption and desorption as rate-determining steps.

Our observations thus permit the following conclusions to be drawn regarding the processes occurring on MgO. Adsorption–desorption involving equilibration occurs on certain sites, with an apparent $E = 6{\cdot}5 \pm 0{\cdot}5$ kcal. mole^{-1}; the equilibration involves dissociation of the oxygen molecule, but the sites are not saturated in the temperature range 17—275° since the reaction rate increases directly as the oxygen pressure. From the adsorption sites a proportion of the ad-atoms migrate over the surface ($E = 7{\cdot}7 \pm 2{\cdot}0$ kcal. mole^{-1}; Part III); in the temperature range where this process controls the exchange the surface concentration of mobile ad-atoms is independent of oxygen pressure (exchange rate pressure-independent). The mobile ad-atoms exchange with oxygen ions in the surface when they reach suitable exchange sites; the apparent activation energy of the exchange process proper, involving a switch of electrons from one oxygen nucleus to another, or from an appropriate defect to the ad-atom, is $36 \pm 1{\cdot}0$ kcal. mole^{-1}, but because of the influence of the non-exponential term this process is only rate-determining below 420°. In considering this picture we note that Becker *J. Phys. Chem.*, 1953, **57**, 153) records that Ashworth has detected with the electron-field emission microscope twin nuclei on tungsten at room temperature in the presence of oxygen; these nuclei appear suddenly on the tungsten surface, gyrate rapidly around each other, and usually disappear simultaneously, but sometimes separate (? dissociate) and wander off independently. Since only single nuclei were observed in the presence of argon, the twin nuclei might well be adsorbed oxygen molecules, which are moderately mobile over the surface and sometimes dissociate. On the other hand, our observations could equally well arise if adsorption–desorption occurred at fixed sites, the ad-atoms remained relatively immobile, and $E = 7{\cdot}7$ kcal. mole^{-1} referred to the mobility of suitable lattice defects, but such immobility of adsorbed oxygen is in our opinion most unlikely (cf. de Boer " Dynamical Character of Adsorption," O.U.P., 1953).

Zinc oxide shows a more complicated state of affairs, the Arrhenius plot for the equilibration reaction showing a break at *ca.* 215°, and the process having an apparent activation energy of 22 ± 1 kcal. mole^{-1} below this temperature and $8{\cdot}5 \pm 1{\cdot}0$ kcal. mole^{-1} above 215°. The higher-temperature line on extrapolation passes satisfactorily through the " high-temperature " exchange reaction points; all processes measured on this oxide vary directly as the oxygen pressure. It seems clear that the process with $E = 8{\cdot}5 \pm 1{\cdot}0$ kcal. mole^{-1}, which is rate-determining in the exchange measurements above 415° for oxide outgassed at 630°, is the surface migration of ad-atoms, which implies that

the oxygen molecule is adsorbed at one site, dissociates, and its component atoms migrate over the surface, undergoing exchange on the way, to other sites where they recombine with other atoms and are desorbed; defect migration appears not possible here because of the pressure-dependence of the process. The " exchange reaction " below 415°, of $E = 27{\cdot}5 \pm 1{\cdot}0$ kcal. mole^{-1} (cf. Part IV), appears to be the true exchange reaction; note, however, that when plotted as $k_0 n_s$ the activation energy becomes 40 ± 2 kcal. mole^{-1}, owing to the change of n_s with temperature. The equilibration reaction below 215°, of $E = 22 \pm 1$ kcal. mole^{-1}, we believe to refer to the adsorption–desorption process: in this connection it is significant that the adsorption measurements in the range 420—520° outlined in Part IV, when separated so far as possible from the reaction with zinc exposed during the outgassing treatment (see Part IV), yield rates which have $E = 15 \pm 6$ kcal. mole^{-1}, and are within a factor of 5 to 10 of those calculated from the slope of the line AB in Fig. 3*b*. In the circumstances, the agreement must be regarded as satisfactory, especially since not every act of adsorption and desorption would be expected

FIGS. 3*a* and 3*b*. *Summary of exchange and equilibration results.*

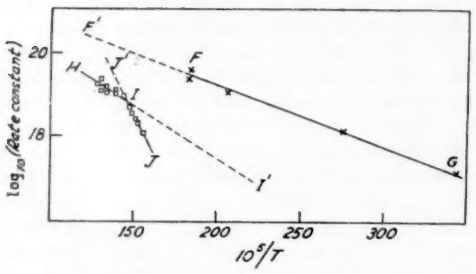


Fig. 3*a*, : MgO, outgassed for *ca.* 16 hr. at 540°. ×, Equilibration. □, Exchange (Part III).

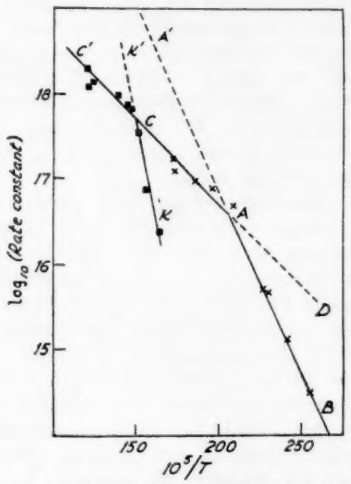


Fig. 3*b*: ZnO, outgassed for *ca.* 16 hr. at 630°. ×, Equilibration. ■, Exchange (Part IV).

to lead to equilibration. Since all processes on this oxide increase directly as the oxygen pressure, it appears that the coverage is small over the whole range of experimental conditions, insofar as saturation is not reached up to at least 15—20 cm.

The processes on zinc oxide are a little difficult to visualise in detail: it appears that adsorption and desorption occur first on an array of active and relatively closely-packed sites ($E \approx 22$ kcal. mole^{-1}), this process leading also to equilibration ($A'AB$, Fig. 3*b*). As the temperature is raised the coverage of these sites increases, as does the speed of equilibration, until the maximum speed possible on these sites is reached at A; thereafter the rate of equilibration (and, at higher temperatures, of exchange) is governed by the rate of migration ($E \approx 8{\cdot}5$ kcal. mole^{-1}) of ad-atoms across the surface to less accessible desorption sites.

We may summarise our findings with reference to Fig. 3: (i) $F'FG$ (MgO) and $A'AB$ (ZnO) — adsorption–desorption

$$\text{Rate} = k_A \mathrm{f}_A(C_g)\phi_A(s)$$
$$\mathrm{f}_A(C_g) \propto p_{\mathrm{O}_2} \text{ for both oxides}$$

$\phi_A(s)$ is some function of the surface; possibly equal to the number of suitable sites per g.

(ii) *HII'* (MgO) and *C'CAD* (ZnO)—migration of ad-atoms or possibly of surface defects (MgO); surface migration of oxygen (ZnO):

$$\text{Rate} = k_M f_M(C_g)\phi_M(s)$$

with the same remarks as above for $\phi_M(s)$; $f_M(C_g) \propto p_{O_2}$ for ZnO but independent of p_{O_2} for MgO.

(iii) *J'IJ* (MgO) and *K'CK* (ZnO)—the true exchange reaction

$$\text{Rate} = k_E f_E(C_g)\phi_E(s)$$

with the same remarks as for the previous case for $f(C_g)$ and $\phi(s)$.

It is not possible to say whether any of the three $f(C_g)$ or $\phi(s)$ terms are the same: hitherto we have used $\phi(n_s)$ instead of $\phi(s)$ but the latter formulation, being more general, seems preferable.

We have insufficient evidence to determine the mechanism of the adsorption stage leading to dissociation; *i.e*, whether the act of adsorption involves dissociation (which seems most likely) or whether this is promoted by bombardment from the gas phase; neither can we say whether on dissociation both oxygen atoms become mobile or if one is bound to the lattice as suggested by Garner *et al.* (*Discuss. Faraday Soc.*, 1950, **8**, 246) for cuprous oxide. Speculation about the exact nature of the exchange step is unprofitable at present; the significant point is the demonstration of appreciable mobility of the surface oxygen in crystalline oxides.

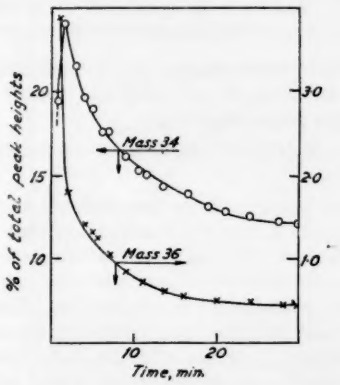


FIG. 4. *Exchange reaction using non-equilibrated oxygen.* MgO at 385°.

Fig. 4 provides direct evidence that the equilibration reaction is much faster than the exchange reaction on MgO; *i.e.*, it gives justification for the extrapolation of *GF* to *F'* in Fig. 3*a*. Fig. 4 shows the 34- and 36-mass peaks as percentages of the total oxygen molecule peaks during the early stages of an *exchange* reaction in which a 1 : 1 mixture of normal and *ca.* 30% ^{18}O oxygen was used. It is seen that in the first 3—4 min. the 36 peak abundance drops very rapidly to around the equilibrium value for *ca.* 15% ^{18}O (*viz.*, 2% of total peaks) while in the same time the 34 peak abundance *rises* to a value near the equilibrium value (*viz.*, 25% of total peaks) before beginning to fall owing to the effect of the exchange reaction. Several such runs have been performed on both oxides in order to check the validity of the technique and argument used in this work; no anomalies were found.

The author thanks Dr. D. R. Llewellyn, of University College, London, for the water containing *ca.* 12% of ^{18}O, and John & E. Sturge Ltd. for laboratory facilities.

1, WHEELEYS ROAD, BIRMINGHAM, 15. [*Received, November 13th*, 1953.]

Dithiols. Part XIII. The Alkaline Hydrolysis of Acetylated Vicinal Hydroxy-thiols.*

By J. S. Harding and L. N. Owen.

[Reprint Order No. 4825.]

The rates of liberation of acetyl and of thiol groups have been determined during the alkaline hydrolysis of partly and fully acetylated derivatives of 2-mercaptoethanol, *trans*-2-mercapto*cyclo*hexanol, *trans*-2-mercapto*cyclo*pentanol, and 2 : 3-dimercaptopropanol. The degree of cyclisation to the corresponding 1 : 2-sulphide is measured by the deficiency in thiol value when deacetylation is complete, and varies from 25 to 90% of the total reaction; with *S*-acetyl derivatives cyclisation is always preceded by migration of acetyl from sulphur to oxygen. The formation of the cyclic sulphide probably occurs by intramolecular displacement of the acetoxy-group (alkyl–oxygen fission) by the neighbouring $-S^-$.

Attempts to synthesise *cis*-2-mercapto*cyclo*hexanol from *trans*-2-acetylthio*cyclo*hexyl toluene-*p*-sulphonate were unsuccessful.

In Part XII* it was shown that the alkaline hydrolysis of certain partly or fully acetylated hydroxy-thiols gave not only the parent hydroxy-thiols but also cyclic sulphides, the latter often preponderating :

$$\text{R·CH(SH)·CH(OH)·R'} \longleftarrow \text{R·CH(SAc)·CH(OAc)·R'} \longrightarrow \text{R·CH(S)CH·R'}$$

It was not possible, from the evidence than presented, to prove the precise course of the overall reaction, but the observation that *cyclo*hexene sulphide, for example, was formed from both the *O*- and the *S*-monoacetyl derivative of *trans*-2-mercapto*cyclo*hexanol suggested that only one of these compounds was the true precursor of the sulphide, and that the other underwent preliminary isomerisation. The purpose of the work now to be described was to study the reaction quantitatively by measuring the rates of liberation of acetyl and thiol groups during the alkaline hydrolysis of various partly or fully acetylated vicinal hydroxy-thiols, and so detect any acetyl migration and determine the proportion of cyclisation for each compound. Non-vicinal compounds, which behave differently, are discussed in the succeeding paper.

The method involved treatment of the derivative with excess of 0·1N-standard alkali in aqueous dioxan at 0°, removal of samples, quenching of the reaction by immediate acidification with standard acid,† back-titration with alkali to determine the acetyl liberated, and finally reacidification and titration with iodine to determine the thiol content of the solution. The formation of a cyclic sulphide involves the disappearance of a thiol group which would otherwise be free; hence any deficiency in the final thiol value from that which would be attained by complete normal hydrolysis corresponds to the amount of cyclisation which has occurred. Apart from polymerisation of the ethylene sulphide, which would not affect the result, the only likely secondary reaction would be ring-fission by free thiol, which is known to occur under vigorous conditions with, *e.g.*, *cyclo*hexene sulphide (Miles and Owen, *loc. cit.*). Under the present conditions such fission probably does not occur to any appreciable extent, but even if it did the result would not be vitiated, because in the reaction

$$\text{R·SH} + \text{>C(S)C<} \longrightarrow \text{>C(SR)·C(SH)<}$$

there is no change in the number of thiol groups.

The results with 2-acetylthioethanol (II) are shown in Fig. 1*a*. The initial rise in thiol value occurs much more rapidly than the liberation of the acetyl group, and clearly indic-

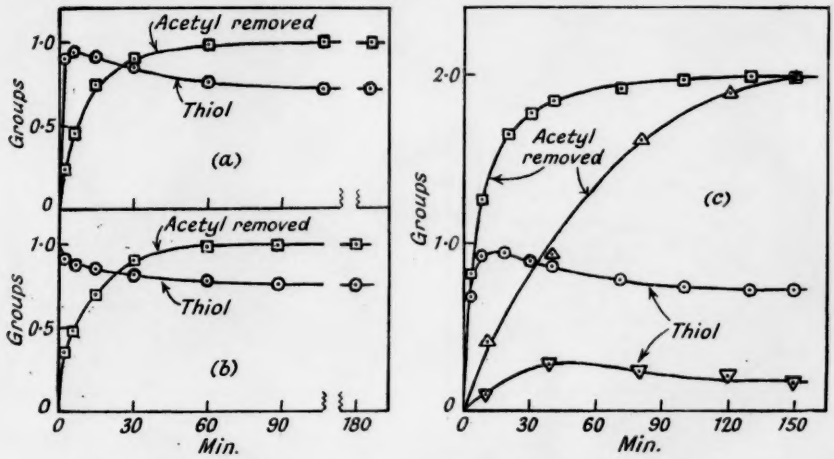
* Part XII, Miles and Owen, *J.*, 1952, 817.

† Acid-catalysed hydrolysis of simple acetates and thiolacetates is very slow compared with alkaline hydrolysis (Böhme and Schran, *Ber.*, 1949, **82**, 453; Schaefgen, *J. Amer. Chem. Soc.*, 1948, **70**, 1308; Rylander and Tarbell, *ibid.*, 1950, **72**, 3021; Noda, Kuby, and Lardy, *ibid.*, 1953, **75**, 913), and control experiments confirmed that no further hydrolysis or migration occurred after acidification.

ates a rearrangement to the *O*-acetate (III) which then undergoes normal hydrolysis (70%) to 2-mercaptoethanol accompanied by cyclisation (30%) to ethylene sulphide (IV); this result is similar, within experimental error, to that observed with 2-mercaptoethyl acetate itself (Fig. 1*b*). The acetyl migration was confirmed by brief treatment of (II) with cold aqueous sodium carbonate, (III) being then isolated in 50% yield. Such rearrangement under mild alkaline conditions has not previously been reported for thiolacetates, although the migration of an acetyl group from sulphur to oxygen has been observed when (II) and similar compounds are heated, especially in the presence of acids (Nylen and Olsen, *Svensk Kem. Tidskr.*, 1941, **53**, 274; Sjöberg, *Ber.*, 1941, **74**, 64; 1942, **75**, 13; Miles and Owen, *loc. cit.*).

With 2-acetylthioethyl acetate (I) rigid interpretation of the result (Fig. 1*c*) is difficult because of the number of possible reactions involved. The almost complete initial liberation of the thiol group suggests at first sight that the *S*-acetyl group is removed first, but taking into account the rapid migration observed with 2-acetylthioethanol the same result

FIG. 1. *Derivatives of 2-mercaptoethanol.*



(*a*) $CH_2(SAc)\cdot CH_2\cdot OH$, 0·0144M. (*b*) $CH_2(SH)\cdot CH_2\cdot OAc$, 0·0123M.
(*c*) $CH_2(SR)\cdot CH_2\cdot OR$ ⊡ ⊙ R = Ac; 0·0131M. △ ▽ R = Bz; 0·0070M.

would evidently arise from a preferential removal of the *O*-acetyl group to give (II), followed by rapid rearrangement to (III). Experimentally, it is impossible to distinguish between these alternatives, and it is probable that both are involved; for unifunctional compounds

$$\underset{\text{(I)}}{CH_2(SAc)\cdot CH_2\cdot OAc} \longrightarrow \underset{\text{(II)}}{CH_2(SAc)\cdot CH_2\cdot OH} \longrightarrow \underset{\text{(III)}}{CH_2(SH)\cdot CH_2\cdot OAc} \longrightarrow \underset{\text{(IV)}}{CH_2{-}CH_2 \atop \quad S \quad}$$

the rate of alkaline hydrolysis of a thiolester is usually about the same as that of the corresponding *O*-ester (Böhme and Schran, *loc. cit.*; Schaefgen, *loc. cit.*; Rylander and Tarbell, *loc. cit.*), and although the presence of a neighbouring acetylthio-group probably facilitates the removal of an acetoxy-group by alkyl–oxygen fission (see discussion on mechanism, below) its effect on normal hydrolysis, which presumably takes place by acyl–oxygen fission, is likely to be less pronounced.

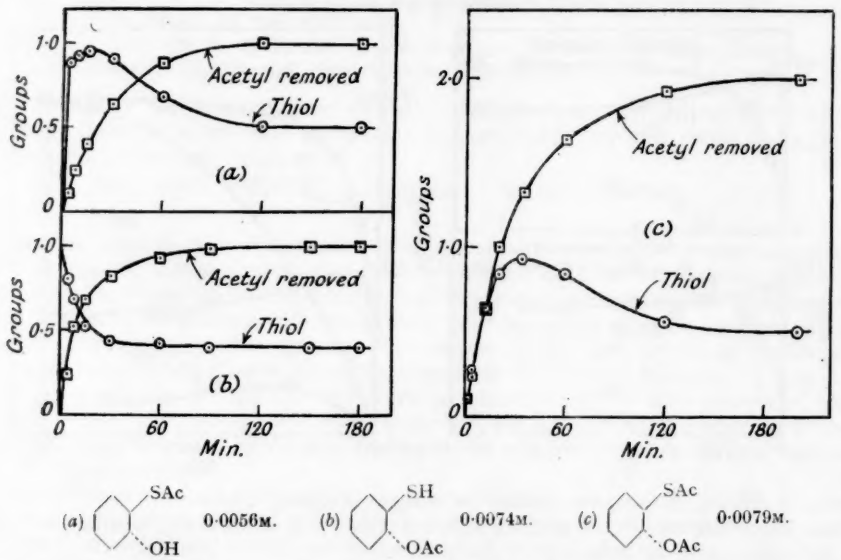
To obtain some preliminary evidence on the possible extension of the cyclisation reaction to other acyl derivatives the dibenzoyl derivative of 2-mercaptoethanol was examined. Under the same conditions as for the diacetyl analogue the rate was much slower, but the final thiol value indicated 85% of cyclisation (Fig. 1*c*). This enhanced degree of elimination is paralleled by the observation (Linstead, Owen, and Webb, *J.*, 1953, 1211) that

under alkaline conditions β-benzoyloxy-esters give a higher proportion of unsaturated acids than do the β-acetoxy-analogues. The di-*p*-nitrobenzoyl derivative was also prepared, but its low solubility precluded its examination under the standard conditions; qualitative tests showed that much ethylene sulphide was formed on treatment with alkali.

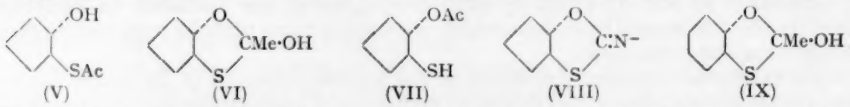
The hydrolyses of the *S*-acetyl, *O*-acetyl, and diacetyl derivatives of *trans*-2-mercapto-*cyclo*hexanol (Fig. 2) followed the same general pattern as those of the mercaptoethanol analogues, and though the acetyl migration (Fig. 2*a*) is slower than that observed with 2-acetylthioethanol (Fig. 1*a*), the degree of cyclisation with the *cyclo*hexane compounds, 50—60%, is considerably greater, probably because of more favourable steric factors.

*cyclo*Pentane compounds often undergo substitution and elimination much more rapidly than their *cyclo*hexane analogues (see, *e.g.*, Owen and Smith, *J.*, 1952, 4026), and it was of interest to find whether this applied also to the cyclisation reaction being studied.

FIG. 2. *Derivatives of* 2-*mercaptocyclohexanol.*



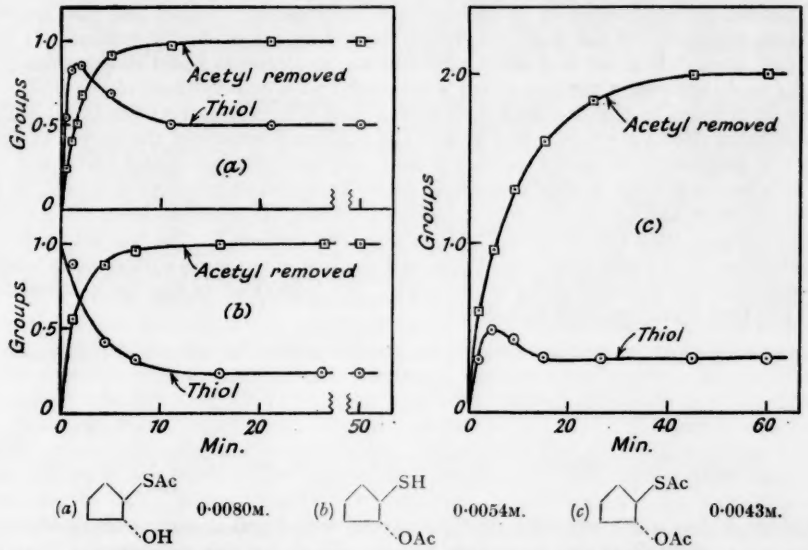
trans-2-Acetylthio*cyclo*pentanol (V) was synthesised by ring-fission of *cyclo*pentene oxide with thiolacetic acid; on acetylation it gave the diacetyl compound, whilst deacetylation with cold methanolic hydrogen chloride yielded *trans*-2-mercapto*cyclo*pentanol and some *cyclo*pentene sulphide. Monoacetylation of the hydroxy-thiol under acid conditions gave *trans*-2-mercapto*cyclo*pentyl acetate (VII). *cyclo*Pentene sulphide was isolated in 20% yield after treatment of (V) with hot aqueous sodium carbonate, much polymer also being formed. Quantitative hydrolysis showed (Fig. 3) that deacetylation of the three acetyl derivatives was much faster than for the *cyclo*hexane analogues. The greater degree of cyclisation undergone by the *O*-acetyl compared with the *S*-acetyl compound agrees with the supposition that the former is the true precursor of the cyclic sulphide; that this



differentiation was less marked in the *cyclo*hexane series, and not evident at all with the derivatives of 2-mercaptoethanol, indicates that in *trans*-2-acetylthio*cyclo*pentanol direct hydrolysis of the *S*-acetyl group competes with acetyl migration more effectively than in

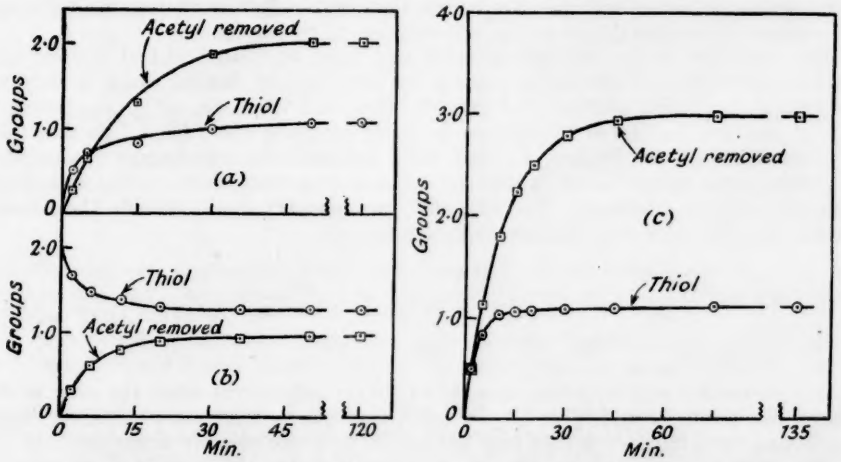
the series previously considered. The fact that migration takes place at all is perhaps surprising, because if it occurs through the usual orthoester intermediate it must involve the

FIG. 3. *Derivatives of 2-mercaptocyclopentanol.*



formation of the strained system (VI) containing two *trans*-fused five-membered rings, whereas in the *cyclo*hexane series a strainless intermediate (IX) is possible. However, although (VI) may be formed less readily than (IX) its highly strained nature probably

FIG. 4. *Derivatives of 2 : 3-dimercaptopropanol.*

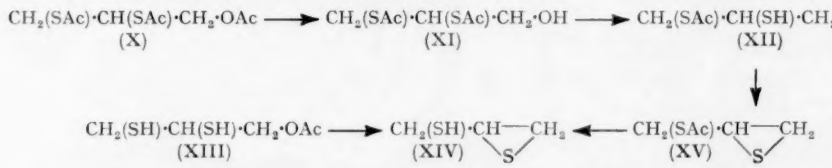


(*a*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OH$, 0·0103M. (*b*) $CH_2(SH)\cdot CH(SH)\cdot CH_2\cdot OAc$, 0·0110M.
(*c*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, 0·0082M.

results in very rapid rearrangement to the *O*-acetate (VII), whereas the *cyclo*hexane compound (IX), being more stable, would rearrange more slowly; the overall result could well be the observed more rapid migration in the *cyclo*pentane series. In his investigations into the preparation of ethylene sulphides by reaction of ethylene oxides with potassium

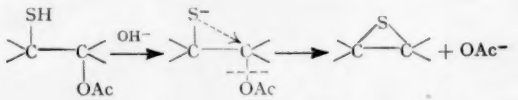
thiocyanate, van Tamelen (*J. Amer. Chem. Soc.*, 1951, **73**, 3444; compare Harding, Miles, and Owen, *Chem. and Ind.*, 1951, 887) postulated the intermediate existence of cyclic oxathiolans, the formation of which was later confirmed by Price and Kirk (*J. Amer. Chem. Soc.*, 1953, **75**, 2396). The failure of the reaction with *cyclo*pentene oxide was attributed by van Tamelen to non-formation of the strained intermediate (VIII), and the structural conditions necessary for the *trans*-fused bicyclic system are evidently critical. It seems likely that even (VI) is not formed in acid solution as attempts failed to isomerise (V) to (VII) by acid catalysis, a method which is successful with 2-acetylthio*cyclo*hexanol.

The hydrolyses of the di-*S*-acetyl, *O*-acetyl, and triacetyl derivatives of 2 : 3-dimercaptopropanol (BAL) are shown in Fig. 4. The relative positions of the curves in Fig. 4*a* prove the occurrence of acetyl migration in 2 : 3-bisacetylthiopropanol (XI), and since mild alkaline hydrolysis of this compound gives 3-acetylthiopropylene sulphide (XV) in high yield (Miles and Owen, *loc. cit.*) it follows that migration occurs from the secondary acetylthio-group, with formation of (XII), which then cyclises.* The triacetyl derivative (X) also gives (XV) under mild conditions, and the first stage in its hydrolysis is probably the removal of the *O*-acetyl group to give (XI); the behaviour of the three acetyl derivatives can thus be summarised as follows :



The lower degree of cyclisation (70%) observed with the *O*-acetate, compared with the di-*S*-acetyl compound (90%) is contrary to the result for the *cyclo*pentane derivatives discussed above, and is probably a consequence of the fact that with the BAL compounds two cyclisation reactions are involved. The *O*-acetate (XIII) contains two free thiol groups, each of which in alkaline solution will exist partly as an anion; the proportion of secondary thiol anion (which, on the basis of the mechanism proposed below, is necessary for cyclisation to occur) will therefore be less than in the alkaline solution of (XII), where the whole of the ionised thiol is in the form suitable for cyclisation.

The formation of the ethylene sulphide ring from acetylated vicinal hydroxy-thiols involves elimination of the acetoxy-group by alkyl–oxygen fission, which is very rare, particularly in alkaline solution (cf. Linstead, Owen, and Webb, *loc. cit.*). In general, this type of fission is facilitated by electron-donating groups in the " alkyl " portion (Balfe, Doughty, Kenyon, and Poplett, *J.*, 1942, 605), and since the transference of electrons in a direction other than that of its covalent bonds occurs much more readily with sulphur than with oxygen (Baddeley, *J.*, 1950, 663) this tendency could provide the necessary driving force for an intramolecular displacement :



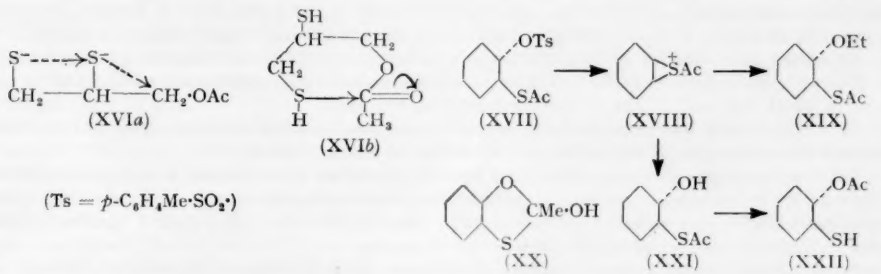
With a monoester of a 1 : 2-diol, epoxide formation only occurs when the ester is of the type which normally undergoes alkyl–oxygen fission (*e.g.*, toluene-*p*-sulphonate, halide); the driving force required is then less, and can be provided even by a neighbouring $-O^-$.

The electron-donating properties of sulphur may also be the cause of the unexpectedly high degree of cyclisation which occurs in the derivatives of 2 : 3-dimercaptopropanol compared with those of 2-mercaptoethanol, in that electron release towards $C_{(1)}$ from the attacking thiol group on $C_{(2)}$ would be reinforced in the dithiol by the similar properties

* Although acetyl migration could occur from the primary group in (XI) (compare 3-acetylthiopropanol, Part XIV, following paper) the derivation of (XII) by two successive migrations, 3 ⟶ 1, 2 ⟶ 3, although possible, appears unlikely.

of the thiol group on $C_{(3)}$, as shown in (XVI*a*). An alternative suggestion, by Dr. L. M. Jackman of this Department, is that in 2 : 3-dimercaptopropyl acetate the sulphur atom on $C_{(3)}$ can chelate with the carbonyl-carbon atom (carrying a fractional positive charge owing to the normal polarisation of the carbonyl group) to give (XVI*b*), in which the thiol group on $C_{(2)}$ may be held in a relatively favourable position for rear attack on $C_{(1)}$. Further evidence on the special reactivity of acetylated hydroxy-dithiols is presented in the succeeding paper.

Formation of the cyclic sulphides from the *trans-cyclo*pentane and *trans-cyclo*hexane derivatives involves an inversion of configuration at the carbon atom carrying the *O*-acetyl group, and it would therefore be of considerable interest to examine the corresponding *cis*-compounds. Winstein, Hess, and Buckles (*J. Amer. Chem. Soc.*, 1942, **64**, 2796) have shown that the monoacetate of *cis-cyclo*hexane-1 : 2-diol can be obtained by reaction of *trans*-2-acetoxy*cyclo*hexyl toluene-*p*-sulphonate with calcium carbonate in moist ethanol. *trans*-2-Acetylthio*cyclo*hexanol was therefore converted into the toluene-*p*-sulphonate (XVII) and treated with those reagents, but the product was 2-acetylthio*cyclo*hexyl ethyl ether (XIX), from which ethyl 2-mercapto*cyclo*hexyl ether was obtained by alkaline hydrolysis. Ether formation was not observed by Winstein, although Owen and Saharia (*J.*, 1953, 2582) obtained a mixture of *cis*-monoacetate and monoacetate-ethyl ether from a similar reaction with *trans*-2-acetoxy*cyclo*heptyl toluene-*p*-sulphonate. In an attempt to circumvent the difficulty, (XVII) was treated with calcium carbonate in moist dioxan, but it gave only *trans*-2-mercapto*cyclo*hexyl acetate (XXII). The different course taken by (XVII) in comparison with the oxygen analogue suggests that elimination of the toluene-*p*-sulphonyloxy-group leads to the sulphonium structure (XVIII) rather than the cyclic *cis*-orthoacetate (XX), which would be the expected intermediate for the formation of a *cis*-monoacetyl derivative; ring-fission of (XVIII) by OEt^- or OH^- would then give (XIX) or (XXI) respectively, and (XXI) would rapidly isomerise to (XXII).



Experimental

The following were prepared by the methods indicated : 2-Acetylthioethanol, b. p. 95°/15 mm., n_D^{20} 1·4720; and 2-mercaptoethyl acetate, b. p. 55°/13 mm., n_D^{17} 1·4658 (Nylen and Olsen, *Svensk Kem. Tidsk.*, 1941, **53**, 274).

2-Acetylthioethyl acetate, b. p. 104°/15 mm., by treatment of 2-mercaptoethanol with excess of acetic anhydride and a trace of sulphuric acid (cf. Rojahn and Lemme, *Arch. Pharm.*, 1925, **263**, 612).

trans-2-Acetylthio*cyclo*hexanol, b. p. 85°/0·002 mm., n_D^{18} 1·5204; and *trans*-2-mercapto-*cyclo*hexyl acetate, b. p. 110°/16 mm., n_D^{20} 1·4870 (Miles and Owen, *J.*, 1952, 817).

trans-2-Acetylthio*cyclo*hexyl acetate, b. p. 132°/10 mm., n_D^{20} 1·4800, in 80% yield from *trans*-2-mercapto*cyclo*hexyl acetate and acetic anhydride–sulphuric acid (cf. Culvenor, Davies, and Heath, *J.*, 1949, 282).

2 : 3-Bisacetylthiopropanol, $\lambda_{max.}$ 2800 Å, ε 7800 (Miles and Owen, *loc. cit.*).

2 : 3-Dimercaptopropyl acetate, b. p. 93—94°/0·8 mm., n_D^{15} 1·5245 (Pavlic, Lazier, and Signaigo, *J. Org. Chem.*, 1949, **14**, 59).

2 : 3-Bisacetylthiopropyl acetate, b. p. 124°/0·1 mm., n_D^{21} 1·5140 (Evans, Fraser, and Owen, *J.*, 1949, 248).

Isomerisation of 2-*Acetylthioethanol with Aqueous Sodium Carbonate*.—2-Acetylthioethanol (2 g.) was stirred at 0° for 8 min. with N-sodium carbonate (200 c.c.). The mixture was then poured into 2N-hydrochloric acid (90 c.c.) at −10°, and quickly extracted with ether (4 × 50 c.c.). Evaporation of the dried ($MgSO_4$) extracts, and distillation of the residue, gave 2-mercaptoethyl acetate (0·89 g.), b. p. 63°/12 mm., n_D^{19} 1·4614 (Found : thiol-S, 26·6. Calc. for $C_4H_8O_2S$: thiol-S, 26·7%). Miles and Owen (*loc. cit.*) record n_D^{20} 1·4612.

2-*Benzoylthioethyl Benzoate*.—To a solution of 2-mercaptoethanol (5 g.) in pyridine (20 c.c.) at 0° benzoyl chloride (20 g.) was slowly added. The mixture was kept at 0° for 5 hr. and then diluted with water and extracted with chloroform. The extracts were washed successively with 2N-sulphuric acid, water, aqueous sodium hydrogen carbonate, and water, and then dried (Na_2SO_4), and evaporated to an oil. Distillation gave a main fraction (6 g.) of the *dibenzoyl* derivative, b. p. 167—177°/0·001 mm., n_D^{18} 1·5965, which solidified, but had m. p. <30° and could not be recrystallised (Found : C, 66·9; H, 4·9; S, 11·0. $C_{16}H_{14}O_3S$ requires C, 67·1; H, 4·9; S, 11·2%). Light absorption in EtOH : max., 2270, 2360, 2640 Å; ε 20,800, 18,600, 8900.

2-p-*Nitrobenzoylthioethyl* p-*Nitrobenzoate*.—Similar treatment of 2-mercaptoethanol (2 g.) in pyridine (50 c.c.) at 0° with *p*-nitrobenzoyl chloride (10·5 g.) for 48 hr. gave a solid when the reaction mixture was diluted with water. Recrystallisation from benzene–light petroleum (b. p. 40—60°) gave the *di*-p-*nitrobenzoate*, flattened needles, m. p. 145° (Found : C, 51·1; H, 3·3; N, 7·6. $C_{16}H_{12}O_7N_2S$ requires C, 51·1; H, 3·2; N, 7·45%). Light absorption in ethanol : max., 2270, 2510, 2580—2660 Å; ε 10,000, 20,700, 24,100.

trans-2-*Acetylthio*cyclo*pentanol*.—A mixture of *cyclo*pentene oxide (Owen and Smith, *loc. cit.*) (10·3 g.) and thiolacetic acid (9·8 g.) was kept at room temperature for 4 days and then distilled, to give trans-2-*acetylthio*cyclo*pentanol* (14·4 g.), b. p. 69°/0·001 mm., n_D^{17} 1·5133 (Found : C, 52·2; H, 7·6; S, 19·5; thiol-S, 0. $C_7H_{12}O_2S$ requires C, 52·5; H, 7·55; S, 20·0%). Light absorption in ethanol : max., 2350 Å; ε 4000. The α-*naphthylurethane*, after recrystallisation from light petroleum (b. p. 100—120°), had m. p. 118° (Found : C, 65·5; H, 6·0; N, 4·4. $C_{18}H_{19}O_3NS$ requires C, 65·6; H, 5·8; N, 4·25%).

Treatment of the thiolacetate with acetic anhydride–sulphuric acid gave trans-2-*acetylthio*-cyclo*pentyl acetate*, b. p. 90°/0·5 mm., n_D^{22} 1·4888 (Found : C, 53·1; H, 7·0; S, 15·7. $C_9H_{14}O_3S$ requires C, 53·45; H, 7·0; S, 15·8%). Light absorption in ethanol : max., 2350 Å; ε 4400.

Attempted Isomerisation of 2-*Acetylthio*cyclo*pentanol*.—(i) The compound (1 g.) was heated at 100° with acetic acid (0·1 c.c.) for 12 hr. Distillation gave only unchanged material (0·75 g.), b. p. 70°/0·01 mm., n_D^{16} 1·5131, which contained no free thiol.

(ii) No free thiol was present in the solution after treatment of the compound (0·7 g.) with ethereal 0·9N-hydrogen chloride (25 c.c.) for 18 hr. at room temperature.

(iii) The compound (1 g.) was shaken at room temperature with aqueous N-sodium carbonate (200 c.c.) for 5 min. under nitrogen. Acidification with hydrochloric acid and extraction with ether gave unchanged material (0·85 g.), b. p. 75—76°/0·2 mm., n_D^{23} 1·5129. Similar results were obtained by treatment for 25 min.

trans-2-*Mercapto*cyclo*pentyl Acetate*.—A solution of 2-acetylthio*cyclo*pentanol (12 g.) in methanolic 0·8% hydrogen chloride (40 c.c.) was kept at room temperature for 4 days. After removal of the solvent and hydrogen chloride under reduced pressure at room temperature, the residue was distilled, to give *cyclo*pentene sulphide (0·95 g.), b. p. 45°/15 mm., n_D^{17} 1·5262, and 2-mercapto*cyclo*pentanol (2·5 g.), b. p. 97°/15 mm., n_D^{17} 1·5180 (Found : thiol-S, 27·2. Calc. for $C_5H_{10}OS$: S, 27·1%). Van Tamelen (*loc. cit.*) records b. p. 69—70°/65 mm., n_D^{25} 1·5222, for *cyclo*pentene sulphide, and b. p. 92—94°/15 mm., n_D^{25} 1·5190, for the hydroxy-thiol.

Treatment of the hydroxy-thiol with phenyl *iso*cyanate gave the *bisphenylurethane*, which was difficult to purify; after several recrystallisations from light petroleum (b. p. 100—120°) it had m. p. 162° (Found : C, 64·5; H, 5·9; N, 8·3. $C_{19}H_{20}O_3N_2S$ requires C, 64·0; H, 5·7; N, 7·9%).

Selective monoacetylation of the hydroxy-thiol (2·1 g.) at room temperature with acetic anhydride (1·9 g.) and sulphuric acid catalyst in the usual way gave, after two distillations, trans-2-*mercapto*cyclo*pentyl acetate* (1·0 g.), b. p. 93—95°/15 mm., n_D^{14} 1·4845 (Found : thiol-S, 19·5; Ac, 27·0. $C_7H_{12}O_3S$ requires S, 20·0; Ac, 26·9%).

Formation of cyclo*Pentene Sulphide by Alkaline Deacetylation of* trans-2-*Acetylthio*cyclo-*pentanol*.—The thiolacetate (3·2 g.) was " steam-distilled " at 60° under reduced pressure with sodium hydrogen carbonate (3 g.) in water (30 c.c.). The solution rapidly became cloudy and oily drops appeared in the distillate. Extraction of the latter with ether, evaporation of the dried ($CaCl_2$) extracts, and distillation of the residue gave *cyclo*pentene sulphide (0·4 g., 20%),

b. p. 125—130°, n_D^{11} 1·5240; another fraction (0·2 g.), b. p. 130—170°, n_D^{11} 1·5115, probably contained some isomerised starting material. The cyclic sulphide was characterised by treatment of a portion (0·1 g.) with methyl iodide (1 g.) for 4 days at room temperature. The trimethylsulphonium iodide (0·1 g.) was collected, washed with acetone, and recrystallised from ethanol; it had m. p. 213°. Culvenor, Davies, and Heath (*loc. cit.*) give m. p. 215°.

Quantitative Deacetylations.—Phenolphthalein, the usual indicator for determination of acetyl values, is unsatisfactory for thiolacetates because of the acidity of the free thiol produced. Conductimetric experiments, in which standard hydrochloric acid containing appropriate amounts of sodium acetate and 2-mercaptoethanol was titrated with sodium hydroxide, showed that the true end-point would be given by an indicator changing colour in the region pH 6·0—7·5; bromocresol-purple was found to be satisfactory, its suitability being confirmed by control experiments in which it showed the same end-point in both the presence and the absence of thiol.

Distilled water was boiled, and cooled under nitrogen before use. Dioxan was purified by successive treatments with hydrochloric acid, potassium hydroxide, and sodium (Vogel, " Textbook of Practical Organic Chemistry," Longmans, 2nd edn., p. 175) and was finally distilled over sodium. The hydrolysing medium, *ca.* 0·1N-sodium hydroxide in aqueous dioxan (1 : 1 by volume), was made and stored under nitrogen, and for each run 250 c.c. of this solution were introduced into the 500-c.c. reaction flask, surrounded with a bath of ice and water, and fitted with a stirrer, thermometer, and nitrogen-inlet. Air was displaced with purified nitrogen, previously saturated with dioxan–water vapour by passage through some of the hydrolysing solution at 0° (neglect of this precaution resulted in appreciable errors caused by volatilisation of solvent from the reaction vessel), a steady stream of the gas being thereafter maintained throughout the run. Stirring was begun, and when the temperature of the solution became constant at 0° the acetyl derivative (0·001—0·003 mole), weighed in a shallow glass tube, was tipped in, followed by the tube itself. At intervals, 25-c.c. portions were withdrawn by pipette, immediately run into 25 c.c. of *ca.* 0·12N-hydrochloric acid and back-titrated with 0·1N-sodium hydroxide, with bromocresol-purple as internal indicator, the titration being carried to the full violet colour. The same solution was then immediately acidified with 2N-hydrochloric acid and titrated with 0·1N-iodine, with starch as internal indicator. Each run was continued until both the acetyl and the thiol value became constant. A blank experiment was performed under the same conditions in the absence of the acetyl compound. In the calculations no allowance was made for the temperature of the samples withdrawn, control experiments having shown that the weight of solution removed by the pipette at 0° differed by less than 0·2% from that removed at 20°.

Control Hydrolysis Under Acid Conditions.—2-Acetylthioethanol (0·08 g.) was dissolved in 2N-hydrochloric acid and titrated with 0·1N-iodine in the presence of starch. The blue colour disappeared after a few minutes, and was restored by further titration, the process being repeated at intervals. The rate of liberation of thiol group thus determined was: 0·05 (25 min.); 0·08 (50 min.); 0·25 (3·5 hr.); 0·61 (21·5 hr.). Thus, in the quantitative experiments in alkaline solution no appreciable migration or hydrolysis occurs after the samples are acidified.

trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate.*—*trans*-2-Acetylthio*cyclo*hexanol (34 g.) and toluene-*p*-sulphonyl chloride (41 g.) in pyridine (200 c.c.) were kept at 0° for 20 hr. On the addition of crushed ice (150 g.) a dark oil separated; this was taken up in chloroform (2 × 100 c.c.), and the extracts were washed in the usual way, dried (Na_2SO_4), and evaporated to an oil. This was dissolved in benzene (100 c.c.), and diluted with light petroleum (b. p. 40—60°) to incipient turbidity at room temperature; after storage at 0° for 3 days the deposited crystals of the *toluene*-p-*sulphonate* (40 g.) were collected. Recrystallisation from the same solvent gave needles, m. p. 58° (Found: C, 54·4; H, 6·4; S, 19·5. $C_{15}H_{20}O_4S_2$ requires C, 54·9; H, 6·1; S, 19·5%).

Reaction of trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate with Calcium Carbonate.*—(i) The toluene-*p*-sulphonate (34 g.) was heated under reflux with calcium carbonate (10 g.), ethanol (200 c.c.), and water (1 c.c.) in a atmosphere of nitrogen for 24 hr. The precipitated calcium toluene-*p*-sulphonate and unchanged calcium carbonate were removed by filtration and washed with ethanol. The combined filtrate and washings were concentrated under reduced pressure to 75 c.c., then diluted with water and extracted with chloroform, to give 2-*acetylthio*cyclo*hexyl ethyl ether* (18·6 g.), b. p. 67—70°/0·0001 mm., n_D^{16} 1·4924 (Found: S, 15·45; thiol-S, nil; thiol-S after alkaline hydrolysis, 15·4; Ac, 21·2. $C_{10}H_{18}O_2S$ requires S, 15·8; Ac, 21·3%).

Treatment of the product (4 g.) with 2N-sodium hydroxide (250 c.c.) at room temperature for 20 hr. under nitrogen, followed by acidification, and extraction with light petroleum (b. p.

40—60°) gave *ethyl* 2-*mercapto*cyclo*hexyl ether* (2·8 g.), b. p. 48—50°/0·5 mm., n_D^{18} 1·4820 (Found : C, 60·1; H, 10·1; S, 19·9; thiol-S, 20·6. $C_8H_{16}OS$ requires C, 60·0; H, 10·1; S, 20·0%).

(ii) The toluene-*p*-sulphonate (5 g.) was heated under reflux with calcium carbonate (1·5 g.), water (0·3 c.c.), and dioxan (25 c.c.) for 4 hr. After filtration, and dilution of the filtrate and washings with water (150 c.c.), extraction with chloroform gave *trans*-2-mercapto*cyclo*hexy acetate (1·4 g.), b. p. 70°/0·01 mm., n_D^{17} 1·4884, characterised as the *phenylurethane*, m. p. 122° (from light petroleum, b. p. 80—100°) (Found : C, 61·1; H, 6·6; N, 5·0. $C_{15}H_{19}O_3NS$ requires C, 61·4; H, 6·5; N, 4·8%), undepressed on admixture with the derivative prepared from authentic mercapto-ester.

cyclo*Hexene Sulphide from* trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate*.—The toluene-*p*-sulphonate (3 g.) was boiled under reflux with sodium hydrogen carbonate (4 g.) and water (20 c.c.) for 3 hr. Steam-distillation, and extraction of the distillate with light petroleum (b. p. 60—80°), gave *cyclo*hexene sulphide (0·05 g.), b. p. 75°/25 mm. A large amount of involatile polymeric material remained after the steam-distillation.

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Organic Chemistry Department, Imperial College of Science and Technology, South Kensington, London, S.W.7. [*Received, November 23rd,* 1953.]

Dithiols. Part XIV. The Alkaline Hydrolysis of Acetylated Non-vicinal Hydroxy-thiols.*

By J. S. Harding and L. N. Owen.

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Quantitative alkaline hydrolyses of partly and of fully acetylated derivatives of (i) 3 : 4-dimercaptobutanol, (ii) 4-mercaptobutanol, (iii) 3-mercaptobutanol, (iv) 3-mercaptopropanol, have shown that cyclisation occurs only with (i); the presence of a dithiol grouping is therefore necessary for the formation of the larger-ring sulphides (compare the formation of ethylene sulphides, preceding paper), and possible reasons for the enhanced reactivity of the dithiol are discussed. Acetyl migration occurs with the *S*-acetyl derivatives of (i), (iii), and (iv), but not (ii); a $C_{(3)} \longrightarrow C_{(1)}$ transference, involving a six-membered orthoacetate intermediate, thus represents the limiting condition for this isomerisation.

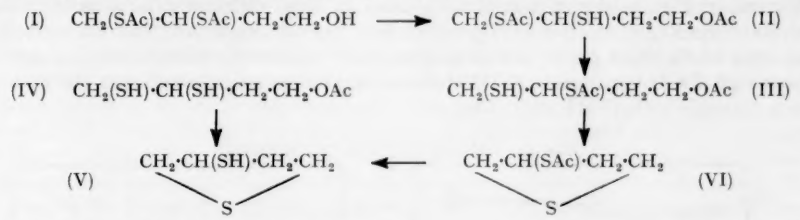
2-Acetoxyethyl 2 : 3-bisacetylthiopropyl ether, and *trans*-2-acetoxy-*cyclo*hexyl 2 : 3-bisacetylthiopropyl ether have been synthesised. These are simple analogues of acetylated 2 : 3-dimercaptopropyl-polyol ethers and 2 : 3-dimercaptopropyl glucoside, and their quantitative alkaline hydrolysis has thrown some light on abnormalities in the deacetylation of the more complex compounds.

The formation of ethylene sulphides by alkaline deacetylation of acetylated vicinal hydroxy-thiols has been discussed in the preceding paper. Miles and Owen (*J.*, 1952, 817) found that similar treatment of the acetyl derivatives of 3 : 4-dimercaptobutanol gave 3-mercaptothiophan (V), but it was not established whether this was a special case (owing to the presence of the dithiol grouping) or whether the reaction was general for the preparation of larger-ring sulphides. The behaviour of these and simpler non-vicinal compounds has therefore been studied by the quantitative method described in Part XIII.

The di-*S*-acetyl (I), *O*-acetyl (IV), and triacetyl derivatives of 3 : 4-dimercaptobutanol gave final thiol values of 1·5, 1·7, and 1·5 groups, corresponding to 50, 30, and 50% cyclisation, respectively (Fig. 1). Under similar conditions the acetyl derivatives of 2 : 3-dimercaptopropanol are hydrolysed about twice as rapidly and undergo a greater degree

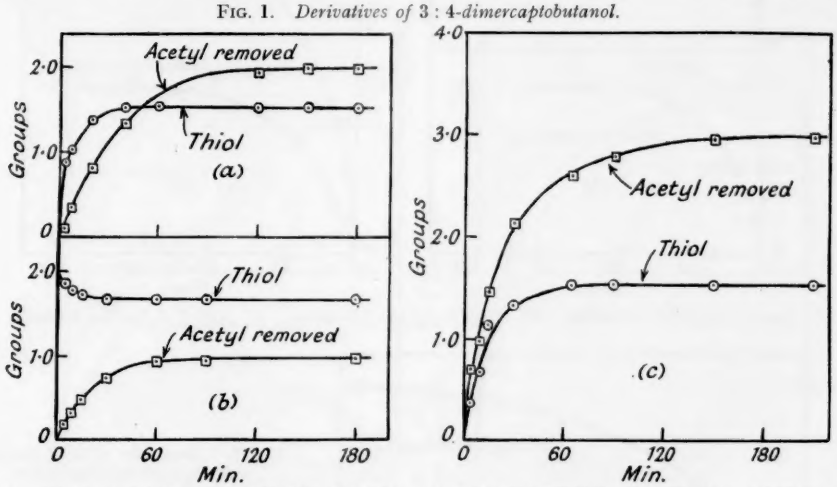
* Part XIII, preceding paper.

of cyclisation (see preceding paper); the interposition of the extra methylene group in 3 : 4-dimercaptobutanol thus considerably reduces the reactivity of the system. In the



early stages of the hydrolysis of (I) the liberation of thiol was more rapid than that of acetyl, indicating the occurrence of acetyl migration. From observations on the hydrolysis of 3- and 4-acetylthiobutanol (see below) this probably affects the secondary group, leading

FIG. 1. *Derivatives of* 3 : 4-*dimercaptobutanol.*



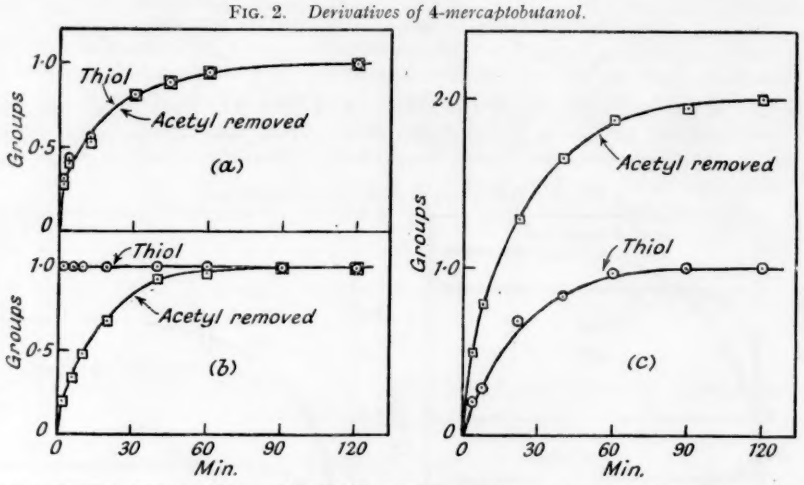
(*a*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot CH_2\cdot OH$, 0·0036M. (*b*) $CH_2(SH)\cdot CH(SH)\cdot CH_2\cdot CH_2\cdot OAc$, 0·0074M. (*c*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot CH_2\cdot OAc$, 0·0030M

to (II), but once this has occurred it is of course possible for the acetyl group on $C_{(4)}$ to migrate to $C_{(3)}$; in this product (III) the thiol group at $C_{(4)}$ is free to attack $C_{(1)}$ by a mechanism analogous to that outlined in the preceding paper, and this would lead *via* 3-acetylthiothiophan (VI) to (V). That the degree of cyclisation is higher with (I) than with (IV) supports such a reaction scheme because it indicates that an intermediate other than (IV) must be involved; the only one possible is (III), and this may cyclise more readily than (IV) for the reason suggested (previous paper) to account for the greater amount of cyclisation with 2 : 3-bisacetylthiopropanol than with 2 : 3-dimercaptopropyl acetate.

The next step was to investigate the acetyl derivatives of 4-mercaptobutanol, from which thiophan would be obtained if cyclisation occurred. 4-Acetylthiobutyl acetate (VII) was prepared by reaction of 4-bromobutyl acetate with potassium thiolacetate. Hydrolysis with aqueous sodium hydroxide gave 4-mercaptobutanol (X) with no thiophan, and the absence of cyclisation was confirmed quantitatively, when the theoretical thiol value for complete normal hydrolysis was attained (Fig. 2*c*). The *S*-acetyl (VIII) and the *O*-acetyl derivative (IX) were obtained by monoacetylation of the hydroxy-thiol under alkaline and acid conditions respectively (cf. Miles and Owen, *loc. cit.*), and they also behaved normally, there being no acetyl migration or cyclisation (Fig. 2*a*, *b*); both compounds were hydrolysed at about the same rate, in conformity with the usual behaviour

of simple acetates and thiolacetates (for references, see preceding paper). Furthermore, since there is no migration, the absence of a discontinuity in the changing slope of the acetyl curve in Fig. 2*c* shows that there is also no large difference between the rates of hydrolysis of the *S*- and the *O*-acetyl group in the diacetyl compound; this is also indicated by the slope of the thiol curve, which is about half that of the acetyl curve at any time. It follows that the two groups in (VII) are behaving independently and that the hydrolysis proceeds through both (VIII) and (IX).

FIG. 2. *Derivatives of* 4-*mercaptobutanol.*



(*a*) AcS·$[CH_2]_4$·OH, 0·0062M. (*b*) HS·$[CH_2]_4$·OAc, 0·0068M. (*c*) AcS·$[CH_2]_4$·OAc, 0·0054M.

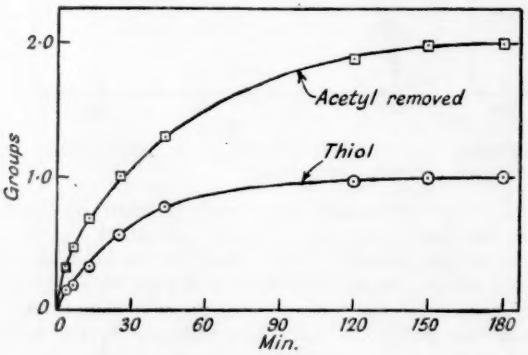
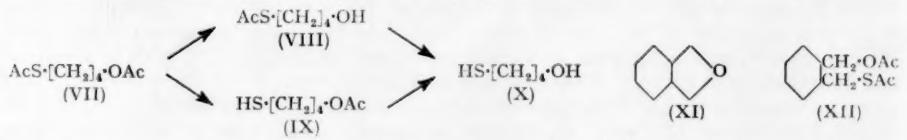


FIG. 3. *Derivative of* cis-2-*mercaptomethyl*cyclo*hexylmethanol.*

0·0053M.

(The *trans* isomer gave almost identical results.)

If the conformation of the carbon chain in 4-mercaptobutanol could be fixed in a favourable position, ring-formation might occur more readily. Haggis and Owen (*J.*, 1953, 389) have shown that the cyclic oxide (XI) can be obtained in both the *cis*- and the

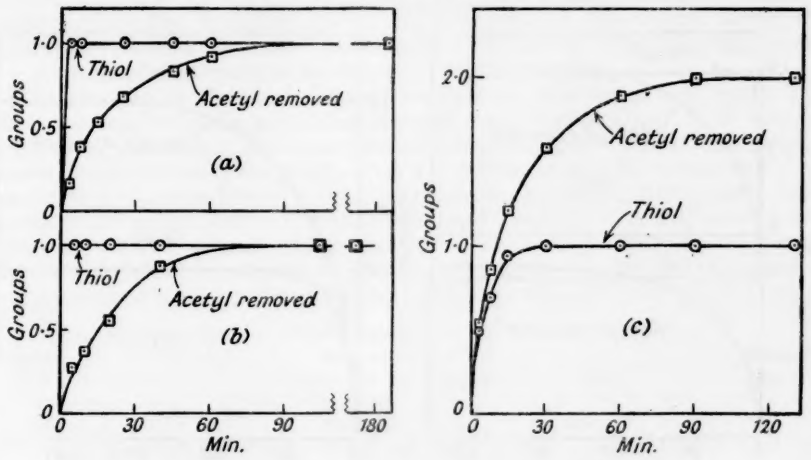


trans-form from certain derivatives of the corresponding diols. Consequently, *cis*- and *trans*-2-(acetylthiomethyl)*cyclo*hexylmethyl acetate (XII), also described by these authors (*ibid.*, p. 408), were examined, but quantitative hydrolysis proceeded normally (Fig. 3)

and showed no migration or cyclisation; *trans*-2-mercaptomethyl*cyclo*hexylmethanol was isolated in good yield by hydrolysis of *trans*-(XII) with aqueous sodium hydroxide.

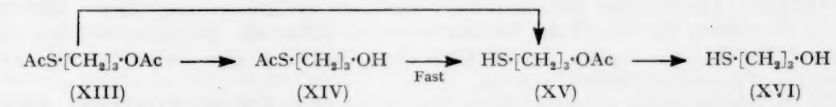
As a typical 1 : 3-hydroxy-thiol, 3-mercaptopropanol was chosen for examination. Addition of thiolacetic acid to allyl alcohol in the presence of ascaridole (Brown, Jones, and Pinder, *J.*, 1951, 2123) gave 3-acetylthiopropanol (XIV) from which 3-acetylthiopropyl acetate (XIII) was obtained by acetylation, and 3-mercaptopropanol (XVI) by hydrolysis with aqueous alkali, no cyclic sulphide being detected. The *O*-acetate (XV) was obtained by monoacetylation of the hydroxy-thiol under acid conditions, and also by rearrangement of (XIV) by heating it in the presence of acetic acid. The latter observation showed that acetyl migration was possible, and when the three derivatives were quantitatively hydrolysed (Fig. 4) the *S*-acetyl compound underwent very rapid isomerization, almost complete liberation of the thiol group having occurred in 3 minutes; the acetyl curve in Fig 4*a* should therefore be practically identical with that of the *O*-acetate, and comparison with Fig. 4*b* shows it to be so. In no case did any cyclisation take place, the final thiol values

FIG. 4. *Derivatives of* 3-*mercaptopropanol.*



(*a*) AcS·[CH$_2$]$_3$·OH, 0·0118M. (*b*) HS·[CH$_2$]$_3$·OAc, 0·0064M. (*c*) AcS·[CH$_2$]$_3$·OAc, 0·0085M.

being the theoretical for complete normal hydrolysis. In the hydrolysis of the diacetyl compound (XIII), deacetylation to the *O*-acetate (XV) can occur by direct loss of the *S*-acetyl group and also by loss of the *O*-acetyl group to give (XIV) followed by rearrangement, but the two routes are indistinguishable experimentally because the migration is so fast. It follows that the final stage in the hydrolysis involves only the reaction (XV) ⟶ (XVI), *i.e.*, liberation of acetyl group with no change in thiol value, which explains why

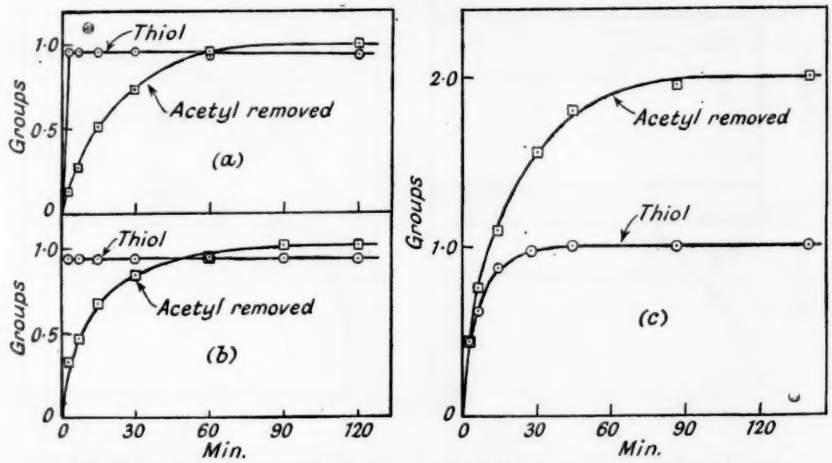


the thiol value in Fig. 4*c* becomes constant before the liberation of acetyl is complete. This is in contrast to the results with 4-acetylthiobutyl acetate (Fig. 2*c*), where, because no acetyl migration occurs, the hydroxy-thiol is formed by two routes (VIII) ⟶ (X) and (IX) ⟶ (X); consequently the thiol and the acetyl value become constant at the same time.

The occurrence of migration in the *S*-acetyl derivative of 3-mercaptopropanol and not in that of 4-mercaptobutanol suggested that the migration observed in 3 : 4-bisacetylthiobutanol involved the 3- and not the 4-*S*-acetyl group, but a more valid comparison required a study of the derivatives of 3-mercaptobutanol. Selective acetylation of the primary

hydroxyl in butane-1 : 3-diol gave 3-hydroxybutyl acetate, which was converted into the crystalline toluene-*p*-sulphonate (XVII). Replacement of a secondary toluene-*p*-sulphonyloxy-group by acetylthio does not always proceed smoothly (cf. Chapman and Owen, *J.*, 1950, 579), but (XVII) readily gave 3-acetylthiobutyl acetate (XVIII), the structure of which was proved by desulphurisation in aqueous alkali by Raney nickel alloy to give *n*-butanol. Alkaline hydrolysis of (XVIII) gave 3-mercaptobutanol, from which 3-mercaptobutyl acetate (XX) and 3-acetylthiobutanol (XIX) were prepared by mono-acetylation under the appropriate conditions, though some difficulty was experienced in the isolation of (XIX) owing to its ease of isomerisation. Brown, Jones, and Pinder (*loc. cit.*) claimed to have obtained it, amongst other products, by addition of thiolacetic acid to crotyl alcohol, but the physical properties of their material correspond more nearly to those of the *O*-acetate (XX); they reported a correct sulphur analysis, but did not record any thiol value. In our hands, repetition of their procedure gave very variable results, and no pure *O*- or *S*-acetyl compound was obtained; from several experiments a considerable quantity of crotyl acetate was isolated, thus providing a further example of

FIG. 5. *Derivatives of* 3-*mercaptobutanol.*



(*a*) $CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OH$, 0·0082M. (*b*) $CH_3{\cdot}CH(SH){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$, 0·0067M.
(*c*) $CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$, 0·0065M.

the acetylating action of thiolacetic acid on alcohols (cf. Stewart and McKinney, *J. Amer. Chem. Soc.*, 1931, **53**, 1482). Brown, Jones, and Pinder suggested crotyl acetate as an intermediate in their reaction scheme, but did not confirm its formation.

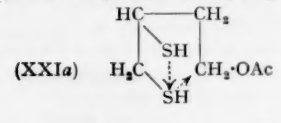
The behaviour of (XIX), (XX), and (XVIII) on quantitative hydrolysis (Figs. 5*a*, *b*, *c*) was very similar to that of the 3-mercaptopropanol derivatives, acetyl migration from the *S*-acetyl group being almost instantaneous; again, no cyclisation took place. With the diacetyl derivative the thiol value became constant before the liberation of acetyl was complete (Fig. 5*c*); the explanation for this is clearly similar to that outlined above for the hydrolysis of 3-acetylthiopropyl acetate.

The cyclisation which occurs with the derivatives of 3 : 4-dimercaptobutanol, but not with those of 4-mercaptobutanol, must depend upon the presence of the extra thiol group, which is itself not directly involved in the reaction. In the preceding paper two possible explanations were given for the high degree of cyclisation obtained with the derivatives of 2 : 3-dimercaptopropanol, and both of these are applicable to the present problem. First, the cyclisation, which involves electron-accession to $C_{(1)}$ from the thiol group on $C_{(4)}$, would be facilitated by the reinforcing electron-donating power of the sulphur atom on $C_{(3)}$, as shown in (XXI*a*); an alternative cyclisation between $C_{(1)}$ and the thiol group on $C_{(3)}$, reinforced by the sulphur on $C_{(4)}$, is also theoretically possible, but formation of a five-

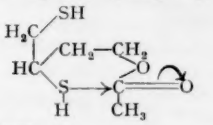
rather than a four-membered ring would undoubtedly be favoured. Secondly, as suggested by Dr. L. M. Jackman, cyclisation may be due to the occurrence of chelation between the sulphur on $C_{(3)}$ and the carbonyl-carbon atom in the acetoxy-group, to give (XXI*b*) in which, with a suitable ring conformation, the thiol group on $C_{(4)}$ might more readily take up a position for rear attack on $C_{(1)}$.

(XVII) $CH_3{\cdot}CH(OTs){\cdot}CH_2{\cdot}CH_2{\cdot}OAc \longrightarrow CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$ (XVIII)

(XIX) $CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OH \longrightarrow CH_3{\cdot}CH(SH){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$ (XX)



(XXI*a*)

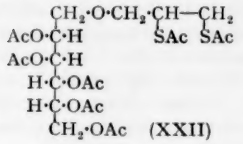


(XXI*b*)

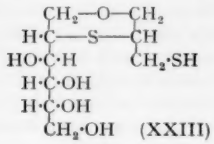
(Ts = *p*-$C_6H_4Me{\cdot}SO_2{\cdot}$)

Acetyl migration in the *S*-acetyl derivatives has been observed with all the 2- and the 3-hydroxy-thiols studied in this and the preceding paper, and presumably occurs through an intermediate five- or six-membered cyclic orthoacetate. The absence of migration with 4-acetylthiobutanol is significant, and must be attributed to the improbability of formation of a seven-membered cyclic orthoacetate.

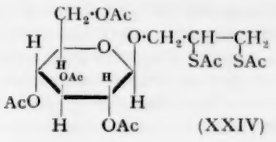
The examples of abnormal alkaline deacetylation recorded in some earlier papers in this series concerned the acetylated glucosides and hexitol ethers of 2 : 3-dimercaptopropanol. Cyclisation in such compounds would probably give a 4-oxathian structure, the six-membered ring being more likely than a larger one, and on the assumption that inversion occurs at $C_{(2)}$ in the hexitol or sugar portion when the acetyl at that position is displaced, the acetylated mannitol ether (XXII) (Bladon and Owen, *J.*, 1950, 591) and the acetylated β-glucoside (XXIV) (Fraser, Owen, and Shaw, *Biochem. J.*, 1947, **41**, 325) would give (XXIII) and (XXV) respectively.* The simple analogues (XXVI) and (XXVII) have now been synthesised in order to detect quantitatively any cyclisation in structures of those types.



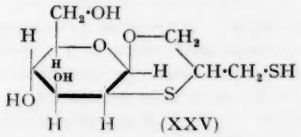
(XXII)



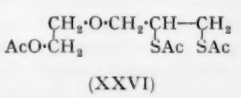
(XXIII)



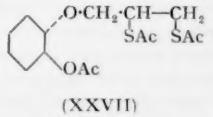
(XXIV)



(XXV)



(XXVI)



(XXVII)

Reaction of ethylene chlorohydrin with sodium allyl oxide gave allyl 2-hydroxyethyl ether, the acetate of which, with bromine, furnished 2-acetoxyethyl 2 : 3-dibromopropyl ether; reaction with potassium thiolacetate then gave 2-acetoxyethyl 2 : 3-bisacetylthiopropyl ether (XXVI). On quantitative alkaline hydrolysis under the standard conditions, the thiol value reached a maximum of 1·9 groups when deacetylation was complete, corresponding to 10% of cyclisation (Fig. 6) On a preparative scale, alkaline deacetylation gave the crude hydroxy-dithiol (crystalline trisphenylurethane), but attempts to isolate the cyclic product were unsuccessful.

Alkoxide-catalysed ring fission of *cyclo*hexene oxide with allyl alcohol gave allyl *trans*-2-hydroxy*cyclo*hexyl ether. Acetylation, addition of bromine, and reaction of the dibromide with potassium thiolacetate gave *trans*-2-acetoxy*cyclo*hexyl 2 : 3-bisacetylthiopropyl ether (XXVII). On quantitative alkaline hydrolysis the thiol value rose to a constant maximum of 1·6 groups when deacetylation was complete (Fig. 6), indicating 40% of cyclisation.

* No abnormality was observed in the deacetylation of the tetra-*O*-methyl analogue of (XXIV), in which such cyclisation cannot occur (Miles and Owen, *J.*, 1950, 2934).

In the deacetylation products from (XXII) and similar hexitol derivatives, the thiol content was usually 85—95% of the total sulphur (Bladon and Owen, *loc. cit.*), *i.e.*, the degree of cyclisation was small; from the glucoside (XXIV), however, the thiol-sulphur in the product was only 60—70% of the total. The behaviour of (XXVI) and (XXVII), thus parallels that of their more complex analogues.

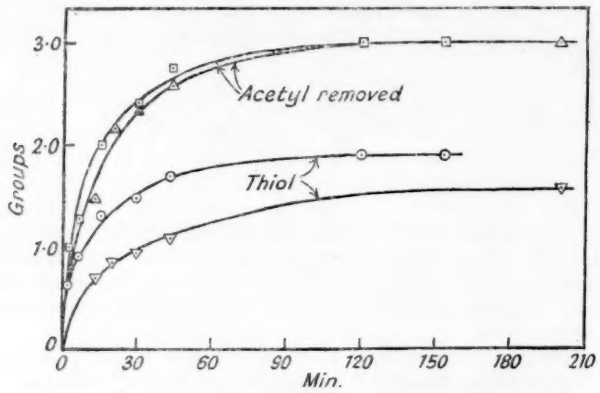
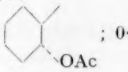


FIG. 6. *Acetylated ethers of 2 : 3-dimercaptopropanol.*
$CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OR$
□ ○ R = $AcO\cdot[CH_2]_3-$; 0·0042M.
△ ▽ R =  ; 0·0025M.

EXPERIMENTAL

3 : 4-Dimercaptobutyl acetate, b. p. 85°/0·002 mm., n_D^{21} 1·5154; 3 : 4-bisacetylthiobutanol, $\lambda_{max.}$ 2280 Å; ε 7800; and 3 : 4-bisacetylthiobutyl acetate, b. p. 137°/0·01 mm., n_D^{21} 1·5137, were prepared by the method of Miles and Owen (*J.*, 1952, 817).

cis-2-(Acetylthiomethyl)*cyclo*hexylmethyl acetate, b. p. 118°/0·2 mm., n_D^{20} 1·4990, was prepared according to Haggis and Owen (*J.*, 1953, 408).

4-*Bromobutyl Acetate*.—To tetrahydropyran (24 g.) containing zinc chloride (10 mg.; anhyd.), acetyl bromide (45 g.) was slowly added at 0°. When the reaction had subsided the mixture was heated under reflux for 1½ hr., then cooled, diluted with chloroform (150 c.c.), and washed with aqueous sodium hydrogen carbonate and with water. Evaporation of the dried (Na_2SO_4) solution gave impure 4-bromobutyl acetate (56·4 g.), b. p. 89—91°/11 mm., n_D^{24} 1·4628 (Found : Br, 44·2. Calc. for $C_6H_{11}O_2Br$: Br, 41·0%). Cloke and Pilgrim (*J. Amer. Chem. Soc.*, 1939, **61**, 2667) obtained a product b. p. 87—93°/15 mm., n_D^{20} 1·4680 (Br, 46·6%), and failed to obtain any material with a lower bromine content.

4-*Acetylthiobutyl Acetate*.—Crude 4-bromobutyl acetate (30 g.), potassium thiolacetate (18·5 g.), and thiolacetic acid (0·5 g.) in ethanol (200 c.c.) were boiled under reflux for 2 hr. The filtered solution was concentrated under reduced pressure, and then diluted with water and extracted with chloroform, to give 4-*acetylthiobutyl acetate* (20 g.) as a pale yellow oil, b. p. 84—86°/0·3 mm., n_D^{20} 1·4724 (Found : C, 50·3; H, 7·6; S, 17·2. $C_8H_{14}O_3S$ requires C, 50·5; H, 7·4; S, 16·8%). Light absorption in EtOH : max., 2270 Å; ε 4600.

4-*Mercaptobutanol*.—The diacetyl compound (9·5 g.) was stirred with 2N-sodium hydroxide (60 c.c.) at room temperature for 3 hr. under nitrogen. Acidification with hydrochloric acid and extraction with chloroform gave 4-mercaptobutanol (4·0 g.) as a colourless liquid, b. p. 102—103°/20 mm., n_D^{19} 1·4870 (Found : C, 45·5; H, 9·5; S, 29·9. Calc. for $C_4H_{10}OS$: C, 45·3; H, 9·5; S, 30·2%). Szarvasi (*Bull. Soc. chim.*, 1950, **463**) records b. p. 99—100°/16 mm., n_D^6 1·491. With phenyl *iso*cyanate it gave the *bisphenylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 128° (Found : C, 62·9; H, 6·1; N, 8·2. $C_{18}H_{20}O_3N_2S$ requires C, 62·8; H, 5·9; N, 8·1%).

4-*Mercaptobutyl Acetate*.—The hydroxy-thiol (1·6 g.), acetic anhydride (1·45 g.) and 10% sulphuric acid in acetic acid (0·1 c.c.) were mixed at 0°, then heated at 60° for an hour, and kept at room temperature for 24 hr. Dilution with water (15 c.c.) and extraction with ether gave 4-mercaptobutyl acetate (1·05 g.), b. p. 125—127°/20 mm., n_D^{18} 1·4634 (Found : thiol-S, 21·2. Calc. for $C_6H_{12}O_2S$: S, 21·6%). Szarvasi (*loc. cit.*) records b. p. 96—98°/15 mm., n_D^{16} 1·467. Treatment with α-naphthyl *iso*cyanate for an hour at 100° gave the *α-naphthylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 76° (Found : C, 64·4; H, 6·3; N, 4·6. $C_{17}H_{19}O_3NS$ requires C, 64·3; H, 6·0; N, 4·4%).

4-*Acetylthiobutanol*.—Acetic anhydride (3 c.c.) was added to 4-mercaptobutanol (3·35 g.) in a solution of sodium hydroxide (1·3 g.) in water (10 c.c.) at 0°. The mixture was stirred for 10 min. and extracted with benzene, to give 4-*acetylthiobutanol* (1·8 g.), b. p. 124°/10 mm., n_D^{13} 1·4905 (Found : C, 48·4; H, 8·4; S, 21·2; thiol-S, 0. $C_6H_{12}O_2S$ requires C, 48·6; H, 8·2; S, 21·6%). Light absorption in EtOH : max., 2280 Å; ε 3600. With phenyl *iso*cyanate for 1 hr. at 100° it gave the *phenylurethane*, m. p. 64° (from light petroleum, b. p. 40—60°) (Found : C, 58·4; H, 6·4; N, 5·6. $C_{13}H_{17}O_3NS$ requires C, 58·4; H, 6·4; N, 5·25%).

trans-2-(*Acetylthiomethyl*)cyclo*hexylmethyl Acetate*.—*trans*-2-Bromomethylcyclohexylmethyl acetate (Haggis and Owen, *J.*, 1953, 389) (22 g.) was heated under reflux for 3 hr. with potassium thiolacetate (10 g.) in ethanol (100 c.c.). Filtration, concentration under reduced pressure, dilution with water, and extraction with chloroform gave *trans*-2-(acetylthiomethyl)cyclohexylmethyl acetate (18·3 g.), b. p. 108°/0·002 mm., n_D^{16} 1·4990 (Found : C, 59·1; H, 8·3; S, 13·0. Calc. for $C_{12}H_{20}O_3S$: C, 59·0; H, 8·25; S, 13·1%). This material was purer than that obtained by Haggis and Owen (*loc. cit.*).

trans-2-*Mercaptomethyl*cyclo*hexylmethanol*.—The above acetate-thiolacetate (14·7 g.) was stirred at room temperature with N-sodium hydroxide (150 c.c.) for 6 hr. under nitrogen. The solution was then acidified with dilute sulphuric acid and extracted with ether, to give the *hydroxy-thiol* (7·6 g.), b. p. 97°/0·2 mm., n_D^9 1·5241 (Found : C, 59·6; H, 10·2; S, 19·8; thiol-S, 19·8. $C_8H_{16}OS$ requires C, 60·0; H, 10·1; S, 20·0%). Treatment with excess of phenyl *iso*cyanate at 100° for 2 hr. gave the *bisphenylurethane* (0·3 g.), which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 127° (Found : C, 66·1; H, 6·7; N, 7·1. $C_{22}H_{26}O_3N_2S$ requires C, 66·3; H, 6·6; N, 7·0%).

3-*Acetylthiopropanol*.—Thiolacetic acid (18 g.) was slowly added, with shaking and cooling, to allyl alcohol (18 g.) containing ascaridole (0·5 c.c.), at 0°. The mixture was kept at room temperature for 2 days and then for 2 hr. at 60°. Distillation gave 3-acetylthiopropanol (23·2 g.), b. p. 57°/0·3 mm., n_D^{18} 1·4938 (Found : C, 44·4; H, 7·7; S, 23·4; thiol-S, 0. Calc. for $C_5H_{10}O_2S$: C, 44·8; H, 7·5; S, 23·85%). Light absorption in EtOH : max., 2320 Å; ε 4300. [Brown, Jones, and Pinder (*J.*, 1951, 2123) record n_D^{20} 1·4827; their product probably contained some *O*-acetyl isomer.] The *phenylurethane* after recrystallisation from light petroleum (b. p. 60—80°) had m. p. 53° (Found : C, 56·5; H, 6·2; N, 5·6. $C_{12}H_{15}O_3NS$ requires C, 56·9; H, 6·0; N, 5·5%).

With excess of acetic anhydride, containing 1% of sulphuric acid, 3-acetylthiopropanol gave 3-acetylthiopropyl acetate, b. p. 120—121°/19 mm., n_D^{23} 1·4720. Light absorption in EtOH : max., 2300 Å; ε 4400. Brown, Jones, and Pinder (*loc. cit.*) give n_D^{20} 1·4720.

3-*Mercaptopropyl Acetate*.—(i) 3-Acetylthiopropanol (15 g.) was stirred at room temperature with 10% aqueous sodium hydroxide (250 c.c.) under nitrogen until the mixture was homogeneous (4 hr.). The solution was acidified with hydrochloric acid and extracted with ether to give 3-mercaptopropanol (5·3 g.), b. p. 87°/14 mm., n_D^{22} 1·4918 (Found : thiol-S, 35·0. Calc. for C_3H_8OS : S, 34·8%). Rojahn and Lemme (*Arch. Pharm.*, 1925, **263**, 612) give b. p. 85—90°/15 mm. A mixture of the hydroxy-thiol (2·85 g.), acetic anhydride (2·9 c.c.), and 10% sulphuric acid in acetic acid (0·1 c.c.) was kept at room temperature overnight, and then diluted with water (15 c.c.) and extracted with ether, to give 3-*mercaptopropyl acetate* (2·25 g.), b. p. 87°/20 mm., n_D^{22} 1·4618 (Found : C, 44·9; H, 7·7; thiol-S, 23·9. $C_5H_{10}O_2S$ requires C, 44·8; H, 7·5; S, 23·85%). Treatment with α-naphthyl *iso*cyanate at 100° for 2 hr. gave the α-*naphthylurethane*, which after recrystallisation from light petroleum (b. p. 60—80°) had m. p. 75° (Found : C, 63·4; H, 5·7; N, 4·5. $C_{16}H_{17}O_3NS$ requires C, 63·4; H, 5·65; N, 4·6%).

(ii) 3-Acetylthiopropanol (3 g.) was heated at 100° with acetic acid (0·1 c.c.) for 48 hr. Dilution with water (5 c.c.) and extraction with ether gave 3-mercaptopropyl acetate (1·8 g.), b. p. 97—99°/30 mm., n_D^{18} 1·4638 (Found : thiol-S, 23·4%).

3-*Hydroxybutyl Acetate*.—A solution of acetic anhydride (51 g.) in pyridine (75 c.c.) was added dropwise during 4 hr. to a stirred solution of butane-1 : 3-diol (45 g.) in chloroform (100 c.c.) and pyridine (75 c.c.), cooled to 0°. After being left at room temperature overnight, the bulk of the solvent was removed under reduced pressure at 40°; the residue was cautiously mixed with concentrated hydrochloric acid (100 c.c.), with cooling, and then extracted four times with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to an oil, distillation of which afforded 3-hydroxybutyl acetate (42 g.), b. p. 102°/18 mm., n_D^{20} 1·4235. Kulpinski and Nord (*J. Org. Chem.*, 1943, **8**, 256) give b. p. 87—89°/13 mm., n_D^{25} 1·4182, for a product assumed to have this structure, obtained by a different method.

3-*Acetylthiobutyl Acetate*.—A solution of 3-hydroxybutyl acetate (30 g.) and toluene-*p*-

sulphonyl chloride (48 g.) in pyridine (150 c.c.) was prepared at 0°, kept thereat overnight, and then concentrated under reduced pressure at 30°. Gradual addition of crushed ice to the residue precipitated an oil, which soon solidified. Recrystallisation of the crude solid (48 g.) from benzene–light petroleum (b. p. 40—60°) gave 3-*toluene*-p-*sulphonyloxybutyl acetate* (38 g.), m. p. 62—63° (Found : C, 54·7; H, 6·5; S, 11·4. $C_{13}H_{18}O_5S$ requires C, 54·5; H, 6·3; S, 11·2%).

This product (20 g.) was boiled under reflux with potassium thiolacetate (10 g.) in ethanol (100 c.c.) for 5 hr., then concentrated under reduced pressure, diluted with water, and extracted with chloroform, to give 3-acetylthiobutyl acetate (8·6 g.), b. p. 52—53°/0·1 mm., n_D^{22} 1·4690 (Found : C, 50·4; H, 7·6; S, 16·85. Calc. for $C_8H_{14}O_3S$: C, 50·5; H, 7·4; S, 16·8%). Light absorption : max., 2320 Å; ε 4200. Brown, Jones, and Pinder (*loc. cit.*) give b. p. 110°/11 mm., n_D^{20} 1·4674, for the product obtained by interaction of thiolacetic acid and crotyl acetate.

Desulphurisation. 3-Acetylthiobutyl acetate (1 g.) and 2N-aqueous sodium hydroxide (20 c.c.) were boiled under reflux until a clear solution was obtained (10 min.). Raney nickel alloy (5 g.) was then added in small portions at a rate sufficient to keep the mixture boiling without the application of heat (15 min.); a filtered test portion then gave no thiol reaction with nitroprusside. Distillation at ordinary pressure gave a first fraction (1·5 c.c.) containing *n*-butanol in suspension; this was characterised as the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 64°.

3-*Mercaptobutanol.*—(i) A solution of 3-acetylthiobutyl acetate (20 g.) in 1% methanolic hydrogen chloride (100 c.c.) was boiled under reflux for 6 hr., then cooled, diluted with chloroform (200 c.c.), washed with water, dried (Na_2SO_4), and evaporated to an oil, distillation of which gave a main fraction (4·8 g.), b. p. 80—90°/16 mm., n_D^{17} 1·4800. Redistillation gave 3-*mercaptobutanol* (3·8 g.), b. p. 90—91°/20 mm., n_D^{16} 1·4816 (Found : C, 44·9; H, 9·7; thiol-S, 30·1. $C_4H_{10}OS$ requires C, 45·2; H, 9·5; S, 30·2%). The *bisphenylurethane*, fine needles from light petroleum (b. p. 100—120°), had m. p. 106° (Found : C, 63·0; H, 5·9; N, 8·3. $C_{18}H_{20}O_3N_2S$ requires C, 62·8; H, 5·9; N, 8·3%).

(ii) 3-Acetylthiobutyl acetate (11 g.) was stirred with 2N-sodium hydroxide (100 c.c.) at room temperature under nitrogen until the mixture became homogeneous (3 hr.). Acidification with dilute sulphuric acid and extraction with chloroform then gave 3-mercaptobutanol (4·2 g.), b. p. 108—109°/25 mm., n_D^{18} 1·4768 (Found : thiol-S, 30·2%).

3-*Mercaptobutyl Acetate.*—A mixture of 3-mercaptobutanol (1·35 g.), acetic anhydride (1·2 g.), and 10% sulphuric acid–acetic acid (0·1 c.c.) was set aside overnight, then diluted with water (10 c.c.) and extracted with ether, to give 3-*mercaptobutyl acetate* (1·1 g.), b. p. 93°/25 mm., n_D^{18} 1·4560 (Found : C, 48·3; H, 8·3; thiol-S, 21·5. $C_6H_{12}O_2S$ requires C, 48·6; H, 8·2; S, 21·6%).

3-*Acetylthiobutanol.*—(i) Acetic anhydride (1·7 g.) was added in one portion to a stirred solution of 3-mercaptobutanol (1·7 g.) and sodium hydroxide (0·7 g.) in water (10 c.c.) at 0°. After 10 min. the solution was extracted with benzene (15 c.c.). Evaporation of the dried extract and distillation of the residual oil gave a main fraction (0·9 g.), b. p. 70—71°/0·5 mm., n_D^{16} 1·4850, consisting essentially of the *S*-acetyl derivative (Found : thiol-S, 1·0; Ac, 29·2. Calc. for $C_6H_{12}O_2S$: Ac, 29·05%). A lower-boiling fraction (0·2 g.), b. p. 45—65°/0·5 mm., n_D^{16} 1·4580, was probably mainly *O*-acetate.

(ii) Thiolacetic acid (9·5 g.) was added to crotyl alcohol (9 g.) containing ascaridole (50 mg.), and the mixture was kept at room temperature for 3 days. Low-boiling material was removed at 40—50°/25 mm., and the residue was then distilled to give : (*a*) 4·75 g., b. p. 50—65°/0·2 mm., which contained much free thiol; and (*b*) 5·5 g., b. p. 70—72°/0·2 mm., n_D^{20} 1·4849, probably a mixture of mono- and di-acetyl derivatives (Found : S, 18·3; thiol-S, 1·0; Ac, 32·4. Calc. for $C_6H_{12}O_2S$: S, 21·6; Ac, 29·05%. Calc. for $C_8H_{14}O_3S$: S, 16·8; Ac, 45·3%). The results could not be reproduced, later experiments giving very much smaller yields of the higher-boiling fractions.

(iii) A mixture of crotyl alcohol (10 g.), thiolacetic acid (12 g.), and ascaridole (0·1 g.) was heated on the steam-bath under reflux for 12 hr. and then distilled, to give mainly low-boiling material (10 g.), b. p. 50—70°/50 mm., redistillation of which furnished crotyl acetate (7 g.), b. p. 130—131°/765 mm., n_D^{20} 1·4150 (Found : sap. equiv., 113. Calc. for $C_6H_{10}O_2$: equiv., 114). The high-boiling residue on distillation gave a main fraction (1·2 g.), b. p. 65—66°/0·5 mm., n_D^{20} 1·4875—1·4955 (Found : S, 19·5; Ac, 47·5%), from which no homogeneous product could be obtained.

2-*Acetoxyethyl Allyl Ether.*—Ethylene chlorohydrin (60 g.) in allyl alcohol (50 c.c.) was added slowly to a boiling solution of sodium (18 g.) in allyl alcohol (200 c.c.), under reflux.

When the addition was complete the mixture was boiled for a further 90 min. and then cooled, neutralised with carbon dioxide, filtered, and evaporated to an oil, distillation of which gave allyl 2-hydroxyethyl ether (42 g.), b. p. 165—170°, n_D^{17} 1·4367. Hurd and Pollack (*J. Amer. Chem. Soc.*, 1938, **60**, 1905) record b. p. 63—64°/18 mm., n_D^{20} 1·4356, for the product obtained by interaction of allyl bromide, ethylene glycol, and sodium.

Treatment of this ether (40 g.) with acetic anhydride (40 c.c.) and a trace of sulphuric acid for 24 hr. at room temperature, followed by dilution with water and extraction with ether, gave *2-acetoxyethyl allyl ether* (41 g.), b. p. 175—177°, n_D^{21} 1·4255 (Found: C, 58·4; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%).

2-Acetoxyethyl 2 : 3-*Dibromopropyl Ether*.—Bromine (50 g.) in carbon tetrachloride (100 c.c.) was added during 2 hr. to a stirred solution of the acetoxy-ether (41 g.) in carbon tetrachloride (100 c.c.) at 0°. Distillation then gave 62 g., b. p. 130—145°/1 mm., n_D^{25} 1·5050—1·4990; redistillation of a middle fraction furnished *2-acetoxyethyl* 2 : 3-*dibromopropyl ether*, b. p. 93°/0·05 mm., n_D^{19} 1·5055 (Found: C, 27·95; H, 4·2; Br, 51·8. $C_7H_{12}O_3Br_2$ requires C, 27·65; H, 4·0; Br, 52·6%).

2-Acetoxyethyl 2 : 3-*Bisacetylthiopropyl Ether*.—The dibromo-compound (40 g.) was boiled under reflux with potassium thiolacetate (37 g.) and thiolacetic acid (0·5 g.) in ethanol (200 c.c.) for 3 hr. Isolation in the usual way gave an oil which was fractionally distilled, 32·1 g. being collected at b. p. 165—168°/0·002 mm. (n_D^{21} 1·5090—1·5137). Redistillation of the middle fraction (13·9 g.) gave *2-acetoxyethyl* 2 : 3-*bisacetylthiopropyl ether*, b. p. 134°/0·0001 mm., n_D^{18} 1·5097 (Found: C, 44·8; H, 6·4; S, 21·5. $C_{11}H_{18}O_5S_2$ requires C, 44·9; H, 6·2; S, 21·8%). Light absorption in EtOH: max., 2290 Å; ε 8800.

2 : 3-*Dimercaptopropyl 2-Hydroxyethyl Ether*.—The triacetyl compound (12 g.) was stirred at room temperature with 2N-sodium hydroxide (200 c.c.) under nitrogen for 2 hr., and then extracted with light petroleum (b. p. 100—120°) to remove unchanged material. The aqueous solution was acidified with hydrochloric acid and extracted with ether to give, on evaporation, crude 2 : 3-dimercaptopropyl 2-hydroxyethyl ether (2·3 g.). This could not be completely purified; the distilled material, b. p. 85—87°/0·0003 mm., n_D^{18} 1·5402, was cloudy, probably because of slight decomposition (Found: S, 35·5; thiol-S, 34·6. Calc. for $C_5H_{12}O_3S_2$: S, 38·1%), but treatment with excess of phenyl *iso*cyanate at 100° for 6 hr. yielded the *trisphenylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 148° (Found: C, 59·6; H, 5·6; N, 7·9. $C_{26}H_{27}O_5N_3S_2$ requires C, 59·4; H, 5·2; N, 8·0%).

*2-Acetoxy*cyclo*hexyl Allyl Ether*.—*cyclo*Hexene oxide (56 g.) and a solution of sodium (2 g.) in allyl alcohol (120 c.c.) were boiled together under reflux for 30 hr. The solution was cooled, neutralised with carbon dioxide, diluted with water, and extracted with ether, to give *allyl 2-hydroxy*cyclo*hexyl ether* (67 g.), b. p. 59°/0·05 mm., n_D^{20} 1·4711 (Found: C, 69·2; H, 10·5. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). The 3 : 5-*dinitrobenzoate*, after recrystallisation from benzene–light petroleum (b. p. 100—120°), had m. p. 84° (Found: C, 55·0; H, 5·4; N, 8·1. $C_{16}H_{18}O_7N_2$ requires C, 54·85; H, 5·2; N, 8·0%). Acetylation of the hydroxy-compound (60 g.) with acetic anhydride (70 c.c.) and a trace of sulphuric acid gave *2-acetoxy*cyclo*hexyl allyl ether* (68 g.), b. p. 63°/0·3 mm., n_D^{19} 1·4557 (Found: C, 66·6; H, 9·2. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·15%).

*2-Acetoxy*cyclo*hexyl* 2 : 3-*Dibromopropyl Ether*.—The above acetoxy-ether (68 g.) in carbon tetrachloride (100 c.c.) was treated with bromine (55 g.) in carbon tetrachloride (100 c.c.) for 2 hr. at 0°, and gave the *dibromide* (98 g.), b. p. 135°/0·0004 mm., n_D^{16} 1·5117 (Found: C, 37·4; H, 5·3; Br, 43·3. $C_{11}H_{18}O_3Br_2$ requires C, 36·9; H, 5·1; Br, 44·6%).

*2-Acetoxy*cyclo*hexyl* 2 : 3-*Bisacetylthiopropyl Ether*.—The dibromide (50 g.) was boiled under reflux with potassium thiolacetate (35 g.) in ethanol (300 c.c.) for 10 hr. Isolation by the usual procedure gave a crude bisthiolacetate (42 g.) which could not be distilled in quantity, owing to decomposition. Distillation of a small sample gave *2-acetox*cyclo*hexyl* 2 : 3-*bisacetylthiopropyl ether*, b. p. 200° (bath)/0·0001 mm., n_D^{14} 1·5151 (Found: C, 51·5; H, 7·0; S, 18·0. $C_{15}H_{24}O_5S_2$ requires C, 51·7; H, 6·9; S, 18·4%). Light absorption in EtOH: max., 2280 Å; ε 7300.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to J. S. H.), and the Medical Research Council for a grant to purchase special chemicals. Absorption spectra were determined by Mrs. A. I. Boston (Spectrographic Laboratory), and analyses were by Mr. F. H. Oliver and his staff (Organic Microanalytical Laboratory).

Department of Organic Chemistry, Imperial College of Science and Technology, South Kensington, London, S.W.7. [*Received, November 23rd*, 1953.]

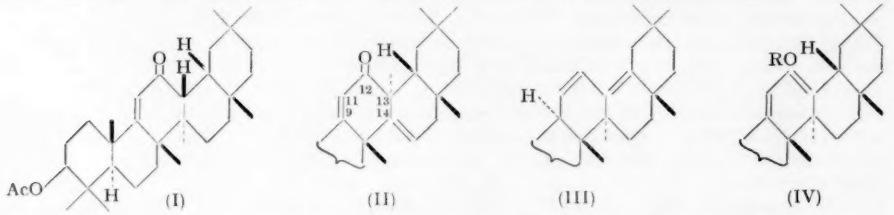
Triterpene Resinols and Related Acids. Part XXIX. The Structure of Oxo-iso-β-amyradienyl Acetate.*

By G. G. Allan, J. D. Johnston, and F. S. Spring.

[Reprint Order No. 4809.]

Wolff–Kishner reduction of oxo-*iso*-β-amyradienyl acetate (followed by acetylation of the product) yields a mixture of two isomeric non-conjugated dienyl acetates (VIII) and (XI), isomerised by hydrochloric–acetic acid to oleana-9(11) : 12-dienyl acetate (V) and oleana-11 : 13(18)-dienyl acetate (III) respectively. A mechanism for the conversion of oxo-*iso*-β-amyradienyl acetate into oleana-11 : 13(18)-dienyl acetate by Clemmensen reduction is based on the observation that oleana-9(11) : 12-dienyl acetate is converted into the 11 : 13(18)-isomer by prolonged refluxing with hydrochloric–acetic acid. Reduction of oxo-*iso*-β-amyradienyl acetate with lithium aluminium hydride (followed by acetylation) gives an *iso*-β-amyradienediol diacetate, which with mineral acid yields a trienyl acetate formulated as (XVII). Catalytic hydrogenation of (XVII) yields an isomer of β-amyrin acetate (*neo*-β-amyrin acetate). It is concluded that oxo-*iso*-β-amyradienyl acetate is correctly formulated as (II).

The discussion included in this paper is a continuation of that in Part XXII (Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019) in which it was shown that Clemmensen reduction of oxo-*iso*-β-amyradienyl acetate, which is obtained from 12-oxo-olean-9(11)-enyl acetate (I) † by oxidation with either bromine or selenium dioxide and was formulated as (II) † by Jeger and Ruzicka (*Helv. Chim. Acta*, 1945, **28**, 209), yields oleana-11 : 13(18)-



(I) (II) (III) (IV)

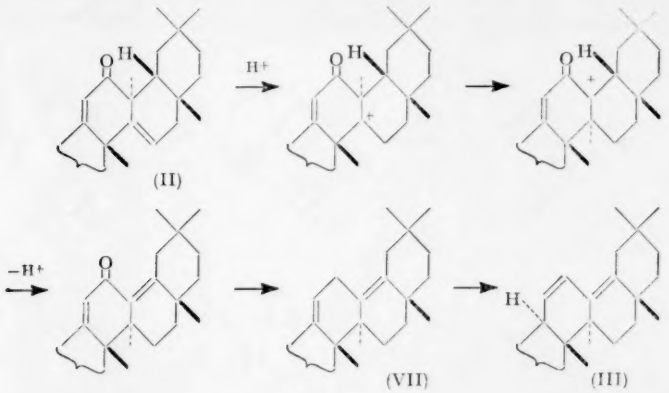
† The relative configurations shown in (I) are those established mainly by Barton and his collaborators (cf. Barton, *J.*, 1953, 1027). The configuration of the 13-methyl group in (II) is considered to be α since the transfer of this group from $C_{(14)}$ to $C_{(13)}$ during the conversion of (I) into (II) must involve its movement across the α-face.

dienyl acetate (III) in high yield. This result, it was contended, did not necessarily indicate that oxo-*iso*-β-amyradienyl acetate is incorrectly formulated by (II) since an alternative view is that the Clemmensen reaction medium induced a reverse methyl migration as shown in the series (II) ⇢ (VII) ⟶ (III). Such a series of changes was considered unlikely, however, since oxo-*iso*-β-amyradienyl acetate is stable to prolonged treatment with strong mineral acid. Arguments against the view that oxo-*iso*-β-amyradienyl acetate has a different carbon skeleton from that of β-amyrin acetate were adduced from the behaviour of the analogous oxo-*iso*-α-amyradienyl acetate and particularly from the observation that catalytic reduction of this compound yields a mixture of ursa-9(11) : 12-dienyl acetate and 12-oxours-9(11)-enyl acetate each of which is a normal ursane derivative (Ruzicka, Ruëgg, Volli, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 140). The experiments described in this paper are limited to those directly bearing on the structure of oxo-*iso*-β-amyradienyl acetate; the chemistry of oxo-*iso*-α-amyradienyl acetate will form the subject of a later paper.

Our first objective was to obtain evidence for or against the presence of an angular methyl group attached to $C_{(13)}$ in oxo-*iso*-β-amyradienyl acetate. It has been shown

* Part XXVIII, *J.*, 1953, 3673.

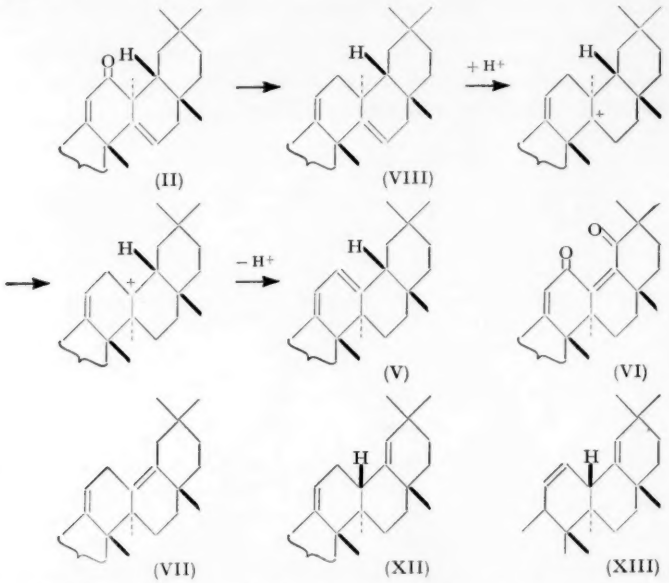
(Budziarek *et al., loc. cit.*) that 12-oxo-olean-9(11)-enyl acetate (I) is readily converted into an enol acetate (IV; R = Ac) and into an enol benzoate (IV; R = Bz). In marked contrast, we find that oxo-*iso*-β-amyradienyl acetate is recovered unchanged after refluxing with acetic anhydride and anhydrous sodium acetate for 172 hr.; it is also recovered unchanged after being heated with the same reagents at 180—200° for 68 hr. and with benzoyl chloride–pyridine at 100° for 10 hr. This stability supports the view that oxo-*iso*-β-amyradienyl acetate carries a methyl substituent at $C_{(13)}$.



Our next objective was to prepare and examine the dienyl acetate corresponding to oxo-*iso*-β-amyradienyl acetate by reductive removal of the carbonyl group. Reduction of oxo-*iso*-β-amyradienyl acetate by the Wolff–Kishner procedure, followed by acetylation, gives a mixture from which two homogeneous products have been isolated. The major product (50%) is an acetate, $C_{32}H_{50}O_2$, m. p. 231°, which gives a yellow colour with tetranitromethane and shows an apparent absorption maximum in the 2000—2250 Å region only; it was recovered unchanged after being shaken in acetic acid solution with hydrogen and platinum at room temperature for 48 hr. It was characterised as homogeneous by alkaline hydrolysis to the corresponding alcohol and regeneration to a product with the same physical constants. Treatment of the acetate, m. p. 231°, with hydrochloric acid in acetic acid gives oleana-9(11) : 12-dienyl acetate (β-amyradienyl-I acetate) (V) in good yield.

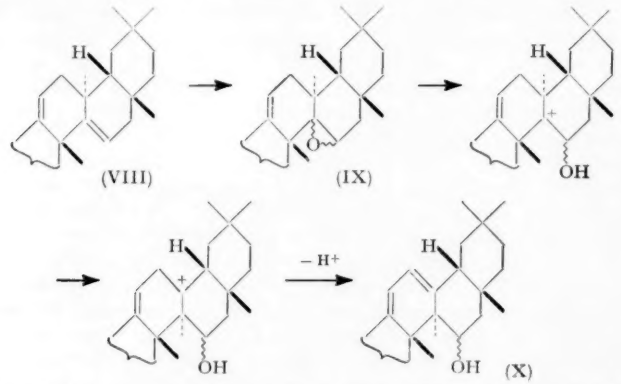
Oxidation of the acetate, m. p. 231°, with selenium dioxide yields 12 : 19-dioxo-β-amyra-9(11) : 13(18)-dienyl acetate (VI), presumably by initial isomerisation to oleana-9(11) : 12-dienyl acetate (V) which gives the dioxodienyl acetate on oxidation with selenium dioxide. We conclude that the acetate, m. p. 231°, is a non-conjugated dienyl acetate. The three possible non-conjugated oleanadienyl acetates, in which the double bonds are in the $C_{(9)}$–$C_{(19)}$ system, are oleana-9(11) : 13(18)- (VII), 9(11) : 18- (XII), and 11 : 18-dienyl acetate (XIII). The acetate, m. p. 231°, differs from oleana-9(11) : 13(18)- and -9(11) : 18-dienyl acetate, each of which has been prepared by unambiguous methods from β-amyrin (Beaton, Johnston, McKean, and Spring, *J.*, 1953, 3660) and each of which yields oleana-11 : 13(18)-dienyl acetate (III) when treated with mineral acid. Furthermore, the ready conversion of the acetate, m. p. 231°, into oleana-9(11) : 12-dienyl acetate (V) shows that it is not the unknown oleana-11 : 18-dienyl acetate since, in analogy with oleana-9(11) : 18-dienyl acetate, oleana-11 : 18-dienyl acetate would be expected to yield the stable oleana-11 : 13(18)-dienyl acetate (III) on treatment with mineral acid. These considerations support the view that the acetate, m. p. 231°, has a different carbon skeleton from that of β-amyrin, *i.e.*, that oxo-*iso*-β-amyradienyl acetate is formed from 12-oxo-olean-9(11)-enyl acetate (I) by a molecular rearrangement. The structure (II) proposed for oxo-*iso*-β-amyradienyl acetate by Ruzicka and Jeger affords a satisfactory explanation of the formation and properties of the dienyl acetate, m. p. 231°. The mechanism (II) ⟶

(VIII) ⟶ (V) for the isomerisation of the acetate, m. p. 231°, which is formulated as (VIII), is proposed.



Oxidation of the acetate, m. p. 231°, with perbenzoic acid gave a product, $C_{32}H_{50}O_3$, which showed the characteristic ultra-violet absorption spectrum of oleana-9(11) : 12-dienyl acetate (max. 2820 Å, ε 9100). The acetate, $C_{32}H_{50}O_3$, contains a secondary alcohol group since mild oxidation with chromic acid converts it into a keto-acetate, $C_{32}H_{48}O_3$, which also shows an intense ultra-violet absorption maximum at 2820 Å. The diol mono-acetate, $C_{32}H_{50}O_3$, and the keto-acetate, $C_{32}H_{48}O_3$, are, like oleana-9(11) : 12-dienyl acetate, strongly dextrorotatory.

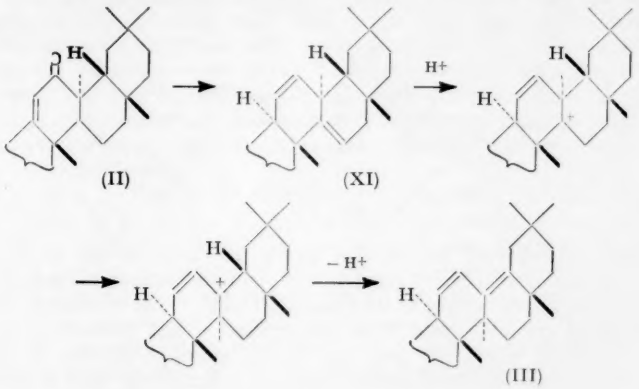
	$[\alpha]_D$	$\lambda_{max.}$	ε
Oleana-9(11) : 12-dienyl acetate	+337°	2820	9000
Oleana-9(11) : 12-diene-3 : 15-diol 3-acetate	+293	2820	9000
15-Oxo-oleana-9(11) : 12-dienyl acetate	+253	2820	9000



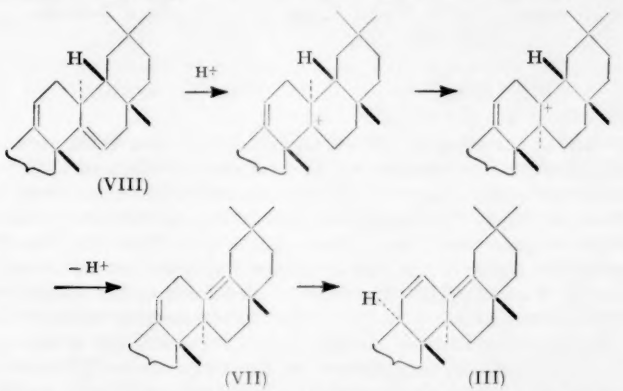
It is probable that treatment of the dienyl acetate (VIII) with perbenzoic acid results in attack of the 14 : 15-double bond to give an unstable oxide (IX), which either spontaneously, or during the isolation procedure, rearranges as shown. The alcohol-

acetate is accordingly considered to be oleana-9(11) : 12-diene-3 : 15-diol 3-acetate (X) and its oxidation product is 15-oxo-oleana-9(11) : 12-dienyl acetate.

The minor reaction product, m. p. 203°, from the Wolff–Kishner reduction of oxo-*iso*-β-amyradienyl acetate is also a non-conjugated dienyl acetate, $C_{32}H_{50}O_2$, which shows ethylenic absorption in the region 2000—2250 Å and gives a positive tetranitromethane test; it differs from oleana-9(11) : 13(18)- (VII) and -9(11) : 18-dienyl acetate. Treatment of the non-conjugated dienyl acetate, m. p. 203°, with hydrochloric acid in acetic acid yields oleana-11 : 13(18)-dienyl acetate (III). The acetate, m. p. 203°, is formulated as (XI) and a mechanism for its conversion into oleana-11 : 13(18)-dienyl acetate (III) is as depicted.

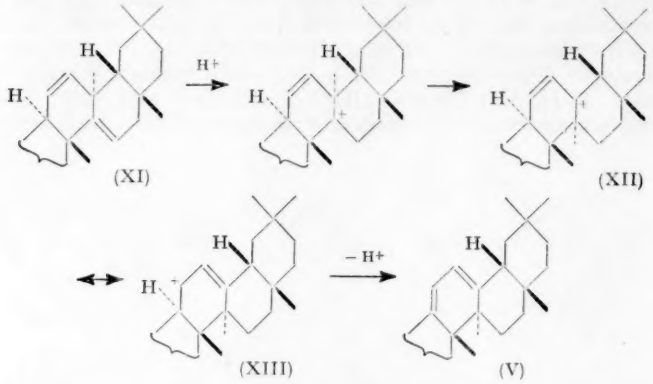


The two non-conjugated dienyl acetates, m. p.s 231° and 203°, obtained by Wolff–Kishner reduction of oxo-*iso*-β-amyradienyl acetate are assigned the structures (VIII) and (XI) respectively, the formation of (VIII) involving simple reduction of the carbonyl group of oxo-*iso*-β-amyradienyl acetate to a methylene group. The genesis of (XI) from oxo-*iso*-β-amyradienyl acetate involves reduction of the carbonyl group with double-bond migration; similar double-bond movements during Wolff–Kishner reductions are well

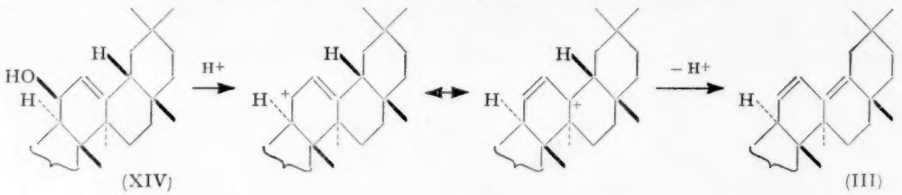


known. The mechanisms suggested above for the acid rearrangements of (VIII) and (XI) require support since an alternative mechanism for the acid rearrangement of (VIII), sketched in (VIII) ⇢ (VII) ⟶ (III), leads to oleana-11 : 13(18)-dienyl acetate (III); the last stage in this sequence has been realised (Beaton *et al.*, *loc. cit.*). The specific allocation of structure (VIII) rather than (XI) to the acetate, m. p. 231°, and consequently of (XI) rather than (VIII) to the acetate, m. p. 203°, rests on considerations which we believe to be compelling. If (VIII) is converted by acid into oleana-11 : 13(18)-dienyl

acetate as shown above, it follows that (VIII) represents the acetate, m. p. 203°, and consequently that the acetate, m. p. 231°, is (XI). In such a case, the conversion of the last acetate into (V) would proceed by the steps (XI) ⇢ (XII) ⟶ (XIII) ⟶ (V).



This mechanism includes an assumption which has been shown to be unwarranted. Reduction of 11-oxo-olean-12-enyl acetate with lithium aluminium hydride yields olean-12-ene-3β : 11β-diol, characterised as its 3-acetate (XIV). The β-configuration is ascribed to the 11-hydroxyl group because it is not acylatable and because on treatment with sodium acetate–acetic anhydride the diol monoacetate is readily dehydrated (*trans*-elimination) to oleana-9(11) : 12-dienyl acetate (V). Relatively mild treatment of (XIV) with mineral acid yields oleana-11 : 13(18)-dienyl acetate (III) and not oleana-9(11) : 12-dienyl acetate (V). It follows that the mechanism shown immediately above is incorrect. These considerations support the view that the non-conjugated dienyl acetate, m. p. 203°, is (XI) and that the non-conjugated dienyl acetate, m. p. 231°, is (VIII).

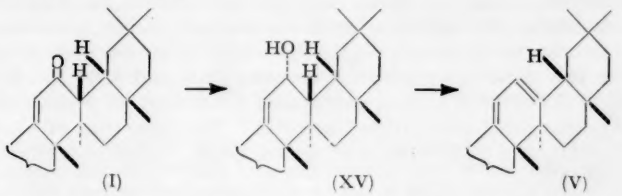


A consideration of the intensity of ultra-violet absorption in the region 2000—2250 Å does not allow differentiation between the two formulæ (VIII) and (XI) for the two non-conjugated dienyl acetates. Since (VIII) contains two triply substituted ethylene bonds, whereas (XI) has one triply substituted and one doubly substituted ethylene bond, it was expected that the former would show more intense absorption in the ethylenic region. The differences in this region are in fact trivial, probably because of vicinal optical effects, particularly in the case of (XI). However, molecular-rotation differences support the choice of (VIII) for the acetate, m. p. 231°; thus the conversion of 12-oxo-olean-9(11) enyl acetate into oxo*iso*-β-amyradienyl acetate is accompanied by a change in $[M]_D$ of approximately —480° and the comparable change from olean-9(11)-enyl acetate to the acetate, m. p. 231°, is accompanied by a $[M]_D$ change of —410°.

The behaviour of the two non-conjugated dienyl acetates with mineral acid raises the question of the mechanism of the conversion of oxo-*iso*-β-amyradienyl acetate into oleana-11 : 13(18)-dienyl acetate by Clemmensen reduction. It is known that simple Clemmensen reduction of 12-oxo-olean-9(11)-enyl acetate (I) proceeds without bond migration (Budziarek *et al., loc. cit.*). If this is the case with oxo-*iso*-β-amyradienyl acetate (II), the non-conjugated dienyl acetate (VIII) would be expected as an intermediate, and this, in the presence of mineral acid, is known to give oleana-9(11) : 12-dienyl acetate (V).

Since the reaction in fact leads to oleana-11 : 13(18)-dienyl acetate (III), either the mechanism of the Clemmensen reduction of (II) does not follow the simple course suggested, or the intermediate oleana-9(11) : 12-dienyl acetate (V) isomerises to the 11 : 13(18)-dienyl acetate (III). Although it is known that the 9(11) : 12-dienyl acetate is stable to relatively vigorous treatment with mineral acid, as shown by its formation from the acetate, m. p. 231°, with hydrochloric–acetic acid, we now find that prolonged treatment of the 9(11) : 12-dienyl acetate (V) with refluxing hydrochloric–acetic acid converts it into oleana-11 : 13(18)-dienyl acetate (III). This satisfactorily accounts for the formation of oleana-11 : 13(18)-dienyl acetate rather than oleana-9(11) : 12-dienyl acetate by the Clemmensen reduction of oxo-*iso*-β-amyradienyl acetate; it does not conflict with our views on either the structure of the dienyl acetate, m. p. 203°, or the mechanism of the conversion of this compound into oleana-11 : 13(18)-dienyl acetate since the acid conditions which complete this change do not isomerise oleana-9(11) : 12-dienyl acetate. In addition, the reaction conditions which convert olean-12-ene-3β : 11β-diol 3-acetate into oleana-11 : 13(18)-dienyl acetate are without effect on oleana-9(11) : 12-dienyl acetate. The reactions of oxo-*iso*-β-amyradienyl acetate described above are uniformly consistent with the view that it is correctly formulated as (II).

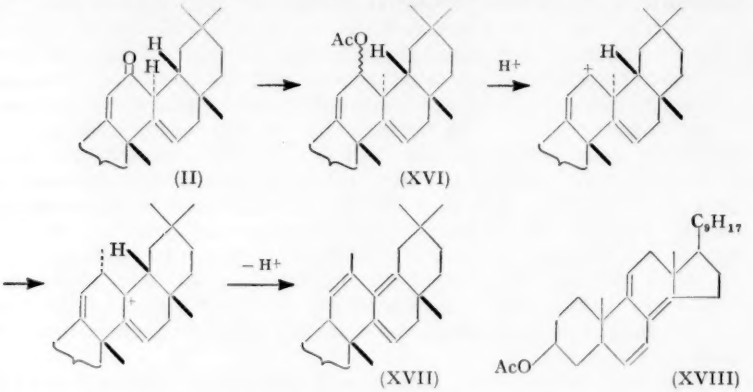
A related reaction leading to the formation of oleana-9(11) : 12-dienyl acetate in acid conditions is worthy of mention. Reduction of 12-oxo-olean-9(11)-enyl acetate (I) with lithium aluminium hydride followed by acetylation gives olean-9(11)-ene-3β : 12α-diol 3-acetate (XV). The configuration of the 12-hydroxyl group is considered to be α because the monoacetate undergoes simple dehydration (*trans*-elimination) when heated with pyridine– or sodium acetate–acetic anhydride, yielding oleana-9(11) : 12-dienyl acetate. When (XV) is treated with acetic–hydrochloric acid in conditions which convert olean-12-ene-3β : 11β-diol 3-acetate into oleana-11 : 13(18)-dienyl acetate, it is converted into oleana-9(11) : 12-dienyl acetate (V).



(I) (XV) (V)

The reduction of oxo-*iso*-β-amyradienyl acetate with lithium aluminium hydride has been described by Budziarek, Johnston, Manson, and Spring, and the product characterised as a diacetate, $C_{34}H_{52}O_4$, now formulated as (XVI); it shows strong ethylenic absorption between 2000 and 2250 Å. This diacetate is also obtained from oxo-*iso*-β-amyradienyl acetate by treatment with alcoholic sodium methoxide at 200°, followed by acetylation. Treatment of the diacetate (XVI) with hydrochloric–acetic acid leads to loss of acetic acid and formation of an acetate, $C_{32}H_{48}O_2$, which shows absorption maxima (in alcohol) at 2280 (ε 18,500), 2820 (ε 16,000), and 2940 Å (ε 12,500), from which we conclude that it is a conjugated trienyl acetate; it is different, however, from oleana-9(11) : 12 : 18-trienyl acetate, the only conjugated trienyl acetate in the oleanane series. The new trienyl acetate is provisionally formulated as (XVII) and contains a crossed chromophore similar to that in ergosta-6 : 8(14) : 9(11) : 22-tetraenyl acetate (XVIII) (Laubach, Schreiber, Agnello, Lightfoot, and Brunings, *J. Amer. Chem. Soc.*, 1953, **75**, 1514) which shows absorption maxima (in ether) at 2325 (log ε 4·25) and 2875 Å (log ε 3·82). The new trienyl acetate in presence of platinum in acetic acid very rapidly absorbs two mols. of hydrogen, to yield an isomer of β-amyrin acetate which we name *neo*-β-amyrin acetate. This is identical with the compound described as *iso*-β-amyradienyl acetate by Budziarek *et al.* (*loc. cit.*) who obtained it by catalytic reduction of either oxo-*iso*-β-amyradienyl acetate or the diacetate $C_{34}H_{52}O_4$. We find that the last two reactions proceed extremely slowly in highly purified acetic acid, rapidly in the presence of a trace of mineral acid. It is our view that a trace of mineral acid is essential for the success of these

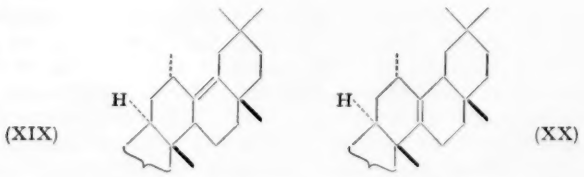
hydrogenolyses and that they proceed *via* the intermediate trienyl acetate. *neo*-β-Amyrin acetate gives an intense orange-red colour with tetranitromethane, and shows absorption



between 2000 and 2250 Å which is very similar to that of olean-13(18)-enyl acetate (δ-amyrin acetate) (see Table: as far as possible the measurements were made under comparable conditions):

	$\lambda_{max.}$	$\varepsilon_{max.}$	ε_{2100}	ε_{2150}	ε_{2200}	ε_{2250}
Olean-12-enyl acetate	2080	3200	3000	1550	520	190
Olean-9(11)-enyl acetate	2070	3100	2200	850	260	185
Olean-13(18)-enyl acetate	2110	5900	—	5100	3500	1800
neo-β-Amyrin acetate	2110	5000	—	4450	3100	1800

That *neo*-β-amyrin acetate is mono- and not di-ethenoid (as assumed by Budziarek *et al.*) was established by oxidation with chromic anhydride, potassium permanganate, or perbenzoic acid to an oxide, $C_{32}H_{52}O_3$, which does not give a colour with tetranitromethane and shows no absorption between 2000 and 3500 Å. When treated with hydrochloric acid the oxide gives a conjugated dienyl acetate which is different from the three known conjugated oleanadienyl acetates. The properties of *neo*-β-amyrin acetate show that it contains a fully substituted double bond; the most probable structures for it are (XIX) and (XX).



Experimental

Rotations were measured in $CHCl_3$ solutions at approx. 15°, and ultra-violet absorption spectra in EtOH with a Unicam SP. 500 spectrophotometer. A light petroleum fraction, b. p. 60—80°, was used for chromatography.

Wolff–Kishner Reduction of Oxo-iso-β-*amyradienyl Acetate.*—A mixture of oxo-*iso*-β-amyradienyl acetate (m. p. 220—221°; 2 g.), methanolic sodium methoxide (from 2 g. of sodium and 25 c.c. of methanol), and hydrazine hydrate (100%; 10 c.c.) was kept at 200° in an autoclave for 13 hr. The crude product was isolated in the usual manner and acetylated on the steam-bath for 2 hr. with pyridine (20 c.c.) and acetic anhydride (20 c.c.). The acetylated product crystallised from methanol–chloroform as plates (1·0 g.), m. p. 228—231° which, after four recrystallisations from the same solvent, yielded the *dienyl acetate*, m. p. 230—231°, $[\alpha]_D$ −9° (*c*, 2·0) (Found: C, 82·2; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). Light absorption: ε_{2120} 5000, ε_{2150} 4180, ε_{2200} 1700, ε_{2250} 320.

Concentration of the original methanol–chloroform mother-liquor yielded a second crop of

plates (0·5 g.), m. p. 175—195°, two recrystallisations of which from chloroform–methanol gave the same dienyl acetate, m. p. and mixed m. p. 230—231° (0·16 g.). Concentration of the mother-liquor from the second crop gave a third crop of plates (0·27 g.), m. p. 180—186°, five recrystallisations of which from chloroform–methanol yielded the isomeric *dienyl acetate*, m. p. 202—203°, $[\alpha]_D$ −95°, −93° (*c*, 1·0, 0·75) (Found: C, 82·6; H, 10·8%). It was recovered unchanged after being shaken in acetic acid with hydrogen and platinum at room temperature for 48 hr. Light absorption: ε_{2100} 5900, ε_{2150} 3700, ε_{2200} 1460, ε_{2250} 430.

Hydrolysis of the Dienyl Acetate, m. p. 230—231°.—The acetate, when refluxed with 3% ethanolic potassium hydroxide for 3 hr., gave a product which separated from methanol as needles, m. p. 193—195°. The *dienol* was obtained after four recrystallisations from methanol as needles, m. p. 195—196°, $[\alpha]_D$ −12° (*c*, 0·8), which gave a yellow colour with tetranitromethane in chloroform. Light absorption in EtOH: Max. at 2110 Å (ε 4500) (Found: C, 84·8; H, 11·4. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Acetylation with acetic anhydride and pyridine followed by crystallisation of the product from methanol–chloroform gave the dienyl acetate as plates, m. p. 230·5—231°, $[\alpha]_D$ −8° (*c*, 2·5); the m. p. was undepressed when mixed with the parent dienyl acetate.

Conversion of the Dienyl Acetate, m. p. 230—231°, *into Oleana*-9(11) : 12-*dienyl Acetate.*—The dienyl acetate (150 mg.) in acetic acid (25 c.c.) was heated with concentrated hydrochloric acid (1 c.c.) on the steam-bath for 4 hr. The product was isolated by means of ether and warmed with acetic anhydride (5 c.c.) and pyridine (5 c.c.) for 1 hr. The acetylated product, isolated by means of ether and crystallised from chloroform–methanol, gave oleana-9(11) : 12-dienyl acetate as needles, m. p. and mixed m. p. 219·5—220°, $[\alpha]_D$ +337° (*c*, 1·5) (Found: C, 82·6; H, 11·1%). Light absorption: Max. at 2820 Å (ε 9000).

Conversion of the Dienyl Acetate, m. p. 202—203°, *into Oleana*-11 : 13(18)-*dienyl Acetate.*—A solution of the acetate (60 mg.) in acetic acid (50 c.c.) and concentrated hydrochloric acid (1 c.c.) was heated on the steam-bath for 7 hr. The product was isolated by means of ether and crystallised thrice from chloroform–methanol to yield oleana-11 : 13(18)-dienyl acetate (35 mg.) as plates, m. p. 227—228°, $[\alpha]_D$ −62° (*c*, 0·6), which gave a red-brown colour with tetranitromethane; a mixture with an authentic specimen prepared by oxidation of β-amyrin acetate with selenium dioxide was undepressed in m. p. Light absorption: Max. at 2420 (ε 22,000), 2510 (ε 27,200), and 2600 Å (ε 17,000). The same treatment of oleana-9(11) : 12-dienyl acetate gave, after two recrystallisations from aqueous acetone, a 70% return of the 9(11) : 12-dienyl acetate, m. p. 215—217°, $[\alpha]_D$ +336° (*c*, 0·7), absorption max. at 2820 Å (ε 9000).

Oxidation of the Dienyl Acetate, m. p. 230—231°, *with Selenium Dioxide.*—A solution of the acetate (0·5 g.) in glacial acetic acid (100 c.c.) was heated under reflux with selenium dioxide (0·5 g.) for 24 hr. The product was isolated by means of ether, and its solution in benzene filtered through a short column of alumina. The solvent was removed from the filtrate and the residue crystallised from chloroform–methanol, to give unchanged dienyl acetate (m. p. and mixed m. p. 230—231°; 50 mg.). The mother-liquor was evaporated to dryness and the residue crystallised from light petroleum (b. p. 60—80°), to yield 2 : 19-dioxo-β-amyra-9(11) : 13(18)-dienyl acetate (200 mg.) as prisms, m. p. 239—242°, which separated from aqueous methanol as square plates, m. p. 240—241°, $[\alpha]_D$ −91° (*c*, 1·5) undepressed in m. p. when mixed with an authentic specimen prepared by oxidation of β-amyrin acetate with selenium dioxide. Light absorption: Max. at 2780 Å (ε 11,700).

Oleana-9(11) : 12-*diene*-3 : 15-*diol* 3-*Acetate.*—A solution of the dienyl acetate, m. p. 230—231° (0·75 g.), in chloroform (35 c.c.) was treated with perbenzoic acid in chloroform (4·6 c.c., 1·3 mol.) at 0° and the solution kept at 0° for 4 days. A solution of the product, which was isolated by means of ether, in light petroleum (b. p. 60—80°)–benzene (3 : 1; 120 c.c.) was filtered through a column (14 × 2 cm.) of activated alumina (Grade I). The column was washed with light petroleum–benzene (3 : 1, 500 c.c.; then 9 : 4, 150 c.c.) which eluted a gum (197 mg.). Continued washing of the column with light petroleum–benzene (3 : 2, 150 c.c.; 9 : 7, 150 c.c.; 1 : 1, 550 c.c.; 2 : 3, 150 c.c.; 1 : 4, 100 c.c.) and with benzene (150 c.c.) eluted crystalline fractions which were combined (289 mg.) and recrystallised from light petroleum and then repeatedly from aqueous methanol, to yield *oleana*-9(11) : 12-*diene*-3 : 15-*diol* 3-*acetate* as plates, m. p. 270—270·5°, $[\alpha]_D$ +293° (*c*, 0·5) (Found: C, 79·6; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). It gives a brown colour with tetranitromethane.

15-*Oxo-oleana*-9(11) : 12-*dienyl Acetate.*—A solution of oleana-9(11) : 12-dien-3 : 15-diol 3-acetate (100 mg.) in glacial acetic acid (50 c.c.) was treated at room temperature with a solution of chromic anhydride (15·4 mg.) in acetic acid (12·5 c.c.), dropwise during 30 min. After 2 hr.

the green solution was diluted with water and the neutral product isolated by means of ether and crystallised from aqueous methanol, to yield 15-*oxo-oleana*-9(11) : 12-*dienyl acetate* (33 mg.) as prismatic needles, m. p. 249—250° $[\alpha]_D$ +252°, +253° (*c*, 0·5, 0·6) (Found: C, 79·9; H, 10·3. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·1%); it gives a red colour with tetranitromethane.

Rearrangement of Oleana-9(11) : 12-*dienyl Acetate to Oleana*-11 : 13(18)-*dienyl Acetate.*—A solution of oleana-9(11) : 12-dienyl acetate (200 mg.; m. p. 215—217°, $[\alpha]_D$ +338°) in acetic acid (100 ml.) was treated with a solution of concentrated hydrochloric acid (10 c.c.) in acetic acid (50 c.c.). The mixture was refluxed for 6 hr. with the addition of concentrated hydrochloric acid (5 c.c.) after 2, 4, and 6 hr. The mixture was set aside overnight and the product was isolated by means of ether and crystallised from chloroform–methanol, to yield oleana-11 : 13(18)-dienyl acetate (100 mg.) as plates, m. p. 224—225°, $[\alpha]_D$ −63° (*c*, 0·6). Light absorption: Max. at 2420 (ε 21,000), 2500 (ε 26,000), and 2600 Å (ε 16,000). A mixture with a specimen prepared by oxidation of β-amyrin acetate with selenium dioxide was undepressed in m. p.

Olean-12-*ene*-3β : 11β-*diol* 3-*Acetate.*—A solution of 11-oxo-olean-12-enyl benzoate (1 g.; m. p. 269—271°, $[\alpha]_D$ +112°) in dry ether (250 c.c.) was treated with lithium aluminium hydride (1 g.) and kept overnight. The product was isolated by means of ether and acetylated by acetic anhydride–pyridine on the steam-bath for 1 hr. The acetylated product separated from chloroform–methanol as needles (900 mg.), m. p. 200—205°, which gave a yellow colour with tetranitromethane. Four recrystallisations gave *olean*-12-*ene*-3β : 11β-*diol* 3-*acetate*, m. p. 209—210°, $[\alpha]_D$ +29° (*c*, 2·2) (Found: C, 79·1; H, 11·2. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Light absorption: Max. at 2100 Å (ε 5600).

Oleana-9(11) : 12-*dienyl Acetate from Olean*-12-*ene*-3β : 11β-*diol* 3-*Acetate.*—The diol monoacetate (250 mg.), anhydrous sodium acetate (400 mg.), and acetic anhydride (30 c.c.) were refluxed for 2 hr. The product was isolated by means of ether and crystallised from aqueous acetone, to give oleana-9(11) : 12-dienyl acetate (120 mg.) as fine needles, m. p. and mixed m. p. 214—217°, $[\alpha]_D$ +338° (*c*, 0·9). Light absorption: Max. at 2820 Å (ε 9000).

Oleana-11 : 13(18)-*dienyl Acetate from Olean*-12-*ene*-3β : 11β-*diol* 3-*Acetate.*—The diol monoacetate (200 mg.) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (0·5 c.c.) on the steam-bath for 5 hr. The product was isolated by using ether and crystallised from chloroform–methanol, to give oleana-11 : 13(18)-dienyl acetate (120 mg.) as plates, m. p. and mixed m. p. 228—230°, $[\alpha]_D$ −62° (*c*, 0·8). Light absorption: Max. at 2500 (ε 29,000), 2420 (ε 24,000), and 2600 Å (ε 19,000).

Olean-9(11)-*ene*-3β : 12α-*diol* 3-*Acetate.*—12-Oxo-olean-9(11)-enyl acetate (1 g.) in dry ether (250 c.c.) was treated with lithium aluminium hydride (1 g.), and the mixture kept overnight. The product was isolated by means of ether (avoiding the use of mineral acid) and acetylated by acetic anhydride–pyridine at room temperature overnight. The acetylated product crystallised from aqueous acetone, to give *olean*-9(11)-*ene*-3β : 12α-*diol* 3-*acetate* (750 mg.) as needles, m. p. 177—178°, $[\alpha]_D$ +36° (*c*, 0·6) (Found: C, 79·51; H, 11·2. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

Oleana-9(11) : 12-*dienyl Acetate from Olean*-9(11)-*ene* 3β : 12α-*diol* 3-*Acetate.*—(*a*) The diol monoacetate (200 mg.), anhydrous sodium acetate (400 mg.), and acetic anhydride (30 c.c.) were refluxed for 2 hr. Crystallisation of the product from aqueous acetone gave oleana-9(11) : 12-dienyl acetate (100 mg.) as needles, m. p. 216—217°, $[\alpha]_D$ +335° (*c*, 0·7). Light absorption: Max. at 2820 Å (ε 9000). A mixture with an authentic specimen, m. p. 219—220°, was undepressed.

(*b*) A solution of the diol monoacetate (200 mg.) in acetic acid (50 c.c.) was heated with concentrated hydrochloric acid (0·5 c.c.) on the steam-bath for 3 hr. The product, isolated by means of ether and crystallised from aqueous acetone, gave oleana-9(11) : 12-dienyl acetate (110 mg.) as needles, m. p. and mixed m. p. 218—219°, $[\alpha]_D$ +338° (*c*, 0·6). Light absorption: Max. at 2820 Å (ε 9000). Oleana-9(11) : 12-dienyl acetate was isolated in similar yield when the solution in acetic acid containing hydrochloric acid was kept overnight at room temperature.

Reduction of Oxo-iso-β-*amyradienyl Acetate with Lithium Aluminium Hydride.*—A solution of oxo-*iso*-β-amyradienyl acetate (0·4 g.) in dry ether (100 c.c.) was refluxed with lithium aluminium hydride (0·3 g.) for 4 hr. The product isolated in the usual way (avoiding the use of mineral acid) was crystallised from aqueous methanol from which iso-β-*amyradienediol* separated as felted needles (0·3 g.), m. p. 202—204°, $[\alpha]_D$ −17° (*c*, 0·8) (Found: C, 81·8; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). The diol gives a yellow colour with tetranitromethane in chloroform.

Acetylation of the diol with pyridine and acetic anhydride gave the diacetate which separates as plates from methanol, m. p. 167—168°, $[\alpha]_D$ +25° (*c*, 1·0), undepressed in m. p. when mixed

with the specimen described by Budziarek *et al.* (*loc. cit.*). Benzoylation yielded iso-β-*amyradienediol dibenzoate*, fine needles (from chloroform–methanol), m. p. 233—234°, $[\alpha]_D$ +70° (*c*, 1·0) (Found: C, 81·6; H, 8·8. $C_{44}H_{56}O_4$ requires C, 81·4; H, 8·7%).

*Reduction of Oxo-*iso*-β-amyradienyl Acetate with Sodium Methoxide.*—A mixture of oxo-*iso*-β-amyradienyl acetate (1·0 g.) and methanolic sodium methoxide (from 1·25 g. of sodium and 15 c.c. of methanol) was kept at 200° in an autoclave for 6 hr. The product was isolated in the usual manner and acetylated by warm acetic anhydride–pyridine. A solution of the dry acetylated product in light petroleum (b. p. 60—80°; 50 c.c.) was filtered through activated alumina (Grade II) (18 × 2 cm.). Light petroleum (900 c.c.) eluted a fraction (500 mg.) which was crystallised from methanol, to yield *iso*-β-amyradienediol diacetate (400 mg.) as square plates, m. p. and mixed m. p. 165—167°, $[\alpha]_D$ +24° (*c*, 1·4) which gave a yellow colour with tetranitromethane.

Treatment of iso-β-*Amyradienediol Diacetate with Hydrochloric Acid.*—A solution of the diol diacetate (1·0 g.) in acetic acid (80 c.c.) was treated with concentrated hydrochloric acid (4 c.c.). After 1 hr., crystalline solid separated from the yellow mixture. Next morning the product was isolated by means of ether, and acetylated by pyridine–acetic anhydride. A solution of the acetylated product (900 mg.) in light petroleum (100 c.c.) was filtered through alumina (Grade I/II) (8·5 × 2 cm.), and the column washed with light petroleum (200 c.c.) and then with light petroleum–benzene (5 : 1; 750 c.c.) which eluted a crystalline solid (550 mg.; m. p. 163°). Crystallisation of this from methanol yielded the *trienyl acetate* as plates, m. p. 168—169°, $[\alpha]_D$ +58° (*c*, 1·0) (Found: C, 82·8; H, 10·2. $C_{32}H_{48}O_2$ requires C, 82·7; H, 10·4%). It gives a purple colour with tetranitromethane.

neo-β-*Amyrin Acetate.*—(*a*) A solution of the trienyl acetate (1·0 g.) in glacial acetic acid was shaken with hydrogen and platinum (from 0·5 g. of PtO_2). Hydrogen absorption was complete after 30 min. (approx. 110 c.c. at N.T.P.). The product, isolated in the usual manner, was crystallised from methanol–chloroform to give *neo*-β-amyrin acetate as needles, m. p. 225—227°, $[\alpha]_D$ +5·0° (*c*, 0·7), undepressed in m. p. when mixed with the specimen described as *iso*-β-amyradienyl acetate by Budziarek *et al.* *neo*-β-Amyrin acetate (m. p. 224—226°; $[\alpha]_D$ +6°) was also obtained by hydrogenation of the trienyl acetate in ethanol over palladised strontium carbonate.

(*b*) A solution of *iso*-β-amyradienediol diacetate (1·0 g.) in purified glacial acetic acid (75 c.c.) was shaken with platinum (from 0·7 g. of PtO_2) and hydrogen. Hydrogen uptake was extremely slow. After 18 hr. one drop of concentrated hydrochloric acid was added and shaking with hydrogen continued. Hydrogen uptake was then rapid. After 6 hr., the product was isolated in the usual manner and crystallised from chloroform–methanol, to yield *neo*-β-amyrin acetate (600 mg.) as needles, m. p. 226—227° undepressed when mixed with the specimen described above. A similar behaviour was observed with oxo-*iso*-β-amyradienyl acetate. When a platinum catalyst and glacial acetic acid were used, reduction of oxo-*iso*-β-amyradienyl acetate was extremely slow (complete after 4 days), the product being *neo*-β-amyrin acetate. Addition of one drop of concentrated hydrochloric acid to the acetic acid solution led to rapid absorption of hydrogen, the reaction being complete in 4 hr. The product was again identified as *neo*-β-amyrin acetate (m. p. and mixed m. p. 224—225°, $[\alpha]_D$ +5°). Hydrolysis of the acetate and benzoylation gave neo-β-*amyrin benzoate* as long needles, m. p. 186—187°, $[\alpha]_D$ +26° (*c*, 3·7) (Found: C, 83·3; H, 10·4. $C_{37}H_{54}O_2$ requires C, 83·7; H, 10·3%).

neo-β-*Amyrin Acetate Oxide.*—(*a*) *neo*-β-Amyrin acetate (0·55 g.) in acetic acid (50 c.c.) was treated at 100° with a solution of chromic oxide (0·25 g.) in water (5 c.c.) and acetic acid (80 c.c.), added dropwise during 30 min. The solution was kept at 100° for 90 min. and the neutral product isolated by means of ether. A solution of the product in light petroleum–benzene (5 : 2, 70 c.c.) was chromatographed on alumina (Grade II; 15 × 2 cm.). Elution with light petroleum–benzene (3 : 2, 200 c.c.) gave a fraction (175 mg.) which after crystallisation from methanol yielded neo-β-*amyrin acetate oxide* as prismatic needles, m. p. 203·5—204·5°, $[\alpha]_D$ −4° (*c*, 1·0) (Found: C, 79·4; H, 10·9. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

(*b*) A solution of *neo*-β-amyrin acetate (0·4 g.) in glacial acetic acid (150 c.c.) was treated with a solution of potassium permanganate (100 mg.) in acetic acid (25 c.c.) added dropwise at room temperature during 30 min. After 1 hr.' stirring the mixture was decolorised by the gradual addition of aqueous sodium hydrogen sulphite, and the product isolated by means of ether. Crystallisation from methanol yielded *neo*-β-amyrin acetate oxide (0·22 g.) as prisms, m. p. 207—208°, $[\alpha]_D$ −6° (*c*, 1·5) (Found: C, 79·3; H, 11·2%). A mixture with the specimen prepared by method (*a*) was undepressed in m. p. The oxide (m. p. 207—208°, $[\alpha]_D$ −5°) was obtained in 60% yield by oxidation of *neo*-β-amyrin acetate with perbenzoic acid in chloroform.

Treatment of neo-β-*Amyrin Acetate Oxide with Hydrochloric Acid* (with L. C. McKean).—A solution of *neo*-β-amyrin acetate oxide (150 mg.) in chloroform (3 c.c.) and glacial acetic acid (20 c.c.) was treated with concentrated hydrochloric acid (2 c.c.) and the mixture kept at room temperature for 18 hr. The neutral product, isolated by means of ether, was acetylated with pyridine–acetic anhydride. A solution of the acetylated product in light petroleum was decolorised by filtration through a short column of alumina. Evaporation of the filtrate followed by crystallisation (4 times) of the solid from aqueous acetic acid gave the *dienyl acetate* as plates, m. p. 192—194°, $[\alpha]_D$ −34° (*c*, 0·85) (Found: C, 82·3; H, 10·8. $C_{32}H_{48}O_2$ requires C, 82·7; H, 10·4%). Light absorption: Max. at 2580 Å (ε 20,000). The dienyl acetate gives a brown colour with tetranitromethane.

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The Royal Technical College, Glasgow. [*Received, November 18th,* 1953.]

Triterpene Resinols and Related Acids. Part XXX. The Oxidation of* 12-*Oxo*iso*oleana*-9(11) : 14-*dienyl Acetate.*

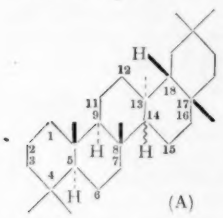
By J. D. Johnston and F. S. Spring.

[Reprint Order No. 4878.]

Oxidation of the pentacyclic 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (I) with perbenzoic acid yields an oxide (II) which on treatment with hydrochloric acid is converted into a hexacyclic derivative with the formation of a new *cyclo*alkane ring. Related compounds are obtained when (I) is oxidised with hydrogen peroxide or when (II) is oxidised with chromic acid. Provisional structures are proposed. Treatment of the oxide (II) with hydrochloric acid gives a chloro-acetate $C_{32}H_{47}O_3Cl$, which on reductive removal of the halogen atom yields an acetate $C_{32}H_{48}O_3$. Wolff–Kishner reduction of the last compound gives an acetate $C_{32}H_{50}O_2$. The presence, in the acetate $C_{32}H_{50}O_2$, of a *cyclo*alkane ring sensitive to mineral acid is inferred, first, from its oxidation by perbenzoic acid to a monoxide $C_{32}H_{50}O_3$ which does not show ethylenic absorption at 2000—2200 Å and, secondly, from its conversion by mineral acid into the normal oleanane derivative, oleana-11 : 13(18)-dienyl acetate (X). A striking resemblance between the acetate $C_{32}H_{48}O_3$, provisionally formulated as (XIX), and "*iso*-α-amyradienonyl-II acetate" obtained from 12-oxo*iso*ursa-9(11) : 14-dienyl acetate (XXII) by treatment with hydrochloric acid is noted and it is suggested that the last reaction also involves the formation of a *cyclo*alkane bridge.

In Part XXIX * it was shown that the behaviour of oxo*iso*-β-amyradienyl acetate on reduction may be satisfactorily interpreted in terms of the expression (I). This compound is now named 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate.

The name *iso*oleanane will be used for the hydrocarbon (A) which is derived from oleanane by the transfer of an angular methyl group from $C_{(14)}$ to $C_{(13)}$. Oxo*iso*-β-amyradienyl acetate becomes 12-oxo*iso*oleana-9(11) : 14-dien-3β-yl acetate (I) and the non-conjugated dienyl acetates obtained from (I) by Wolff–Kishner reduction (Part XXIX) are *iso*oleana-9(11) : 14- (m. p. 231°) and -11 : 14-dien-3β-yl acetate (m. p. 203°) respectively. A similar nomenclature is adopted for oxo*iso*-α-amyradienyl acetate (XXI) which is now named 12-oxo*iso*ursa-9(11) : 14-dienyl acetate.



(A)

The experiments described in this paper were started at the same time as the reduction experiments and were also originally designed to test the validity of the expression (I).

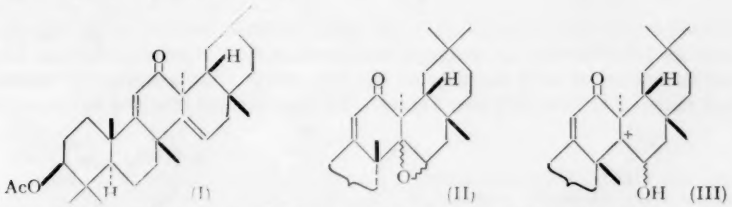
* Part XXIX, preceding paper.

Oxidation of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate, $C_{32}H_{48}O_3$, with hydrogen peroxide in acetic acid gives as major product an acetate $C_{32}H_{48}O_4$ (diol monoacetate) which does not give a colour with tetranitromethane, shows selective absorption in the ultra-violet with an intense maximum at 2360 Å, and is hydrolysed by alkali to the diol, $C_{30}H_{46}O_3$. The oxygen atom introduced has been characterised as a hydroxyl group since the acetate, $C_{32}H_{48}O_4$, on acetylation, yields a diacetate, $C_{34}H_{50}O_5$, and on oxidation with chromic acid at room temperature yields a keto-acetate, $C_{32}H_{46}O_4$; this in turn was characterised by hydrolysis to the corresponding keto-alcohol, $C_{30}H_{44}O_3$, reacetylation of which yields the parent keto-acetate. The diol and the keto-acetate have been prepared by alternative methods from 12-oxo*iso*olean-9(11) : 14-dienyl acetate, as described below.

Oxidation of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (I) with perbenzoic acid, with potassium permanganate or, in sufficiently mild conditions, with chromic acid, gives 14 : 15-epoxy-12-oxo*iso*olean-9(11)-enyl acetate (II). This, in contrast to (I), does not give a colour with tetranitromethane, and shows the ultra-violet absorption spectrum characteristic of an αβ-unsaturated ketone, from which we conclude that it is formed from (I) by the saturation of the isolated ethylenic linkage. This conclusion is supported by the fact that both show the intense absorption band associated with an αβ-unsaturated ketone group but only (I) shows the absorption between 2050 and 2200 Å associated with the presence of an isolated ethylenic bond. The oxide is stable to cold alkali, but when heated therewith yields the alcohol-oxide, reactylation of which regenerates (II).

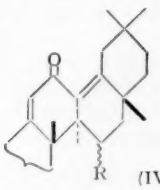
With hydrochloric acid 14 : 15-epoxy-12-oxo*iso*olean-9(11)-enyl acetate (II) yields a chloro-acetate, $C_{32}H_{47}O_3Cl$, which has been directly related to the diol monoacetate obtained by hydrogen peroxide oxidation of (I); alkaline hydrolysis of the chloro-compound gives the diol, $C_{30}H_{46}O_3$, obtained by similar hydrolysis of the diol monoacetate.

The keto-acetate, $C_{32}H_{46}O_4$, obtained by vigorous oxidation of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (I) with chromic acid, is similarly obtained from 14 : 15-epoxy-12-oxo*iso*olean-9(11)-enyl acetate (II).

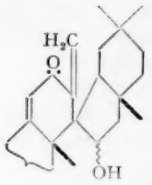


The conversions of (I) into the diol monoacetate and of the oxide (II) into the chloro-acetate, $C_{32}H_{47}O_3Cl$, can be represented as proceeding *via* the ion (III) which, although capable of rearrangement, must achieve stability by the ultimate loss of a proton with the consequent formation of an ethylenic bond or its equivalent; in the latter conversion, this change is probably followed by the replacement of the $C_{(15)}$-hydroxyl group by chlorine. The chloro-acetate, $C_{32}H_{47}O_3Cl$, the related diol monoacetate, $C_{32}H_{48}O_4$, and the keto-acetate, $C_{32}H_{46}O_4$, do not contain an isolated ethylenic linkage. Thus they do not give a colour with tetranitromethane and they are stable to per-acid. Furthermore, whilst their absorption spectra contain strong absorption bands at 2360 Å, they do not show the absorption in the region 2050—2200 Å characteristic of an isolated ethylene bond. Treatment of the chloro-acetate, $C_{32}H_{47}O_3Cl$, with collidine leads to the elimination of hydrogen chloride and the formation of an acetate, $C_{32}H_{46}O_3$, the absorption spectrum of which shows a band at 2320 Å (αβ-unsaturated ketone) and an apparent maximum at 2090 Å (ε 3000) attributed to an isolated ethylene bond; as expected, the acetate, $C_{32}H_{46}O_3$, gives a yellow colour with tetranitromethane. In our view an observation of considerable significance in the elucidation of the structure of the diol monoacetate and its congeners is that the double bond introduced by the removal of the elements of hydrogen chloride from the chloro-acetate is not conjugated with the original chromophore, and cannot be brought into conjugation with it, the acetate $C_{32}H_{46}O_3$ being recovered unchanged after treatment with hydrochloric acid.

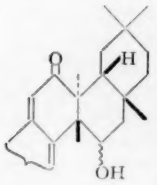
The possibility that the diol monoacetate and its related compounds contain a conjugated dienone group has been excluded by a number of considerations. Rearrangement of the ion (III) could give rise to one of the conjugated dienones (IV; R = OH), (V), and (VI); (VI) is excluded since this would show an intense absorption maximum at approximately 2900 Å (cf. 3α-hydroxy-12-oxochola-7 : 9(11)-dienoic acid, 2920 Å; Fieser, Rajagopalan, Wilson, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 4133) whereas the diol monoacetate exhibits an intense absorption maximum at 2360 Å. Structure (V) is excluded because the related chloro-acetate is recovered unchanged after treatment with ozone. Again, the stability of the related keto-acetate to chromic acid in boiling acetic acid makes such a structure extremely unlikely. Equally cogent reasons, in our opinion, lead to the view that the diol monoacetate cannot be (IV; R = OH). Treatment of the related chloro-acetate with activated zinc dust and acetic acid converts it into the diol diacetate, $C_{34}H_{50}O_5$, by replacement of the chlorine atom by an acetoxy-group; however, mild reduction with zinc in ether–ethanol gives a compound, $C_{32}H_{48}O_3$, by replacement of chlorine by hydrogen. Like the parent chloro-acetate, the compound, $C_{32}H_{48}O_3$, shows an intense absorption maximum at approximately 2340 Å. If (IV; R = Cl) correctly represented the chloro-acetate, the compound, $C_{32}H_{48}O_3$, would be 12-oxo-oleana-9(11) : 13(18)-dienyl acetate (IV; R = H), but this compound has been prepared by an unambiguous method (Beaton, Johnston, McKean, and Spring, *J.*, 1953, 3660) and differs markedly.



(IV)



(V)



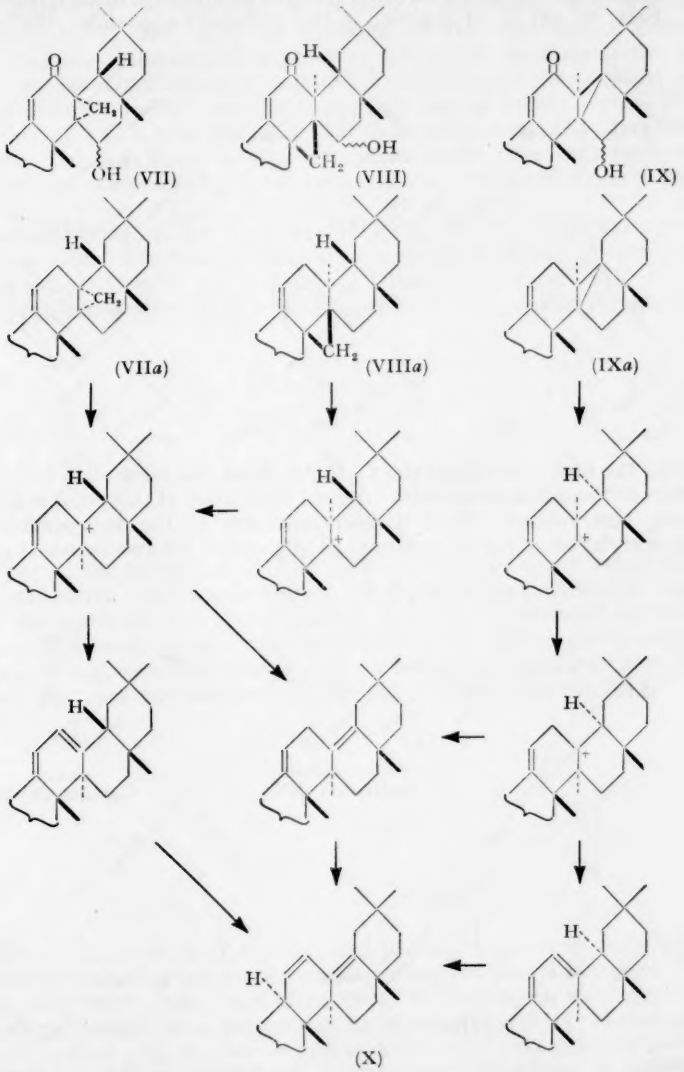
(VI)

In contrast to 12-oxo*iso*oleana-9(11) : 14-dienyl acetate and its oxide, the diol monoacetate and its relatives are all strongly dextrorotatory. Furthermore, the ultra-violet absorption maximum of each member of the last group is at a somewhat shorter wavelength than those of (I) and (II) (see Table). Further insight into the nature of this well-

		$[\alpha]_D$ (in $CHCl_3$)	$\lambda_{max.}$ (Å) (in EtOH)	ε
12-Oxo*iso*oleana-9(11) : 14-dienyl acetate (I)	$C_{32}H_{48}O_3$	− 38°	2450	10,100
12-Oxo*iso*oleana-9(11) : 14-dienol	$C_{30}H_{46}O_2$	− 51	—	—
14 : 15-Epoxy-12-oxo*iso*olean-9(11)-enyl acetate (II)	$C_{32}H_{48}O_4$	− 12·5	2400	10,800
14 : 15-Epoxy-12-oxo*iso*olean-9(11)-enol	$C_{30}H_{46}O_3$	− 26	2420	14,000
Diol monoacetate	$C_{32}H_{48}O_4$	+155	2360	13,400
Diol diacetate	$C_{34}H_{50}O_5$	+141	2360	11,500
Diol	$C_{30}H_{46}O_2$	+167	2360	12,500
Chloro-acetate	$C_{32}H_{47}O_3Cl$	+117	2360	11,100
Keto-acetate	$C_{32}H_{46}O_4$	+ 94	2360	13,000
Keto-alcohol	$C_{30}H_{44}O_3$	+ 71	2360	13,000
Acetate	$C_{32}H_{48}O_3$	+130	2340	11,500
Acetate	$C_{32}H_{46}O_3$	+117	2320	12,500

defined series of compounds was obtained from a study of their behaviour on reduction. As indicated above, reduction of the acetate, $C_{32}H_{47}O_3Cl$, with zinc in a neutral solvent, gives an αβ-unsaturated keto-acetate, $C_{32}H_{48}O_3$. Wolff–Kishner reduction of the last compound yields an acetate, $C_{32}H_{50}O_2$; unlike the parent acetate, $C_{32}H_{48}O_3$, this gives a yellow colour with tetranitromethane and its ultra-violet absorption spectrum is consistent with the presence of a $>C{:}CH-$ linkage. The acetate, $C_{32}H_{50}O_2$, is also obtained as one product of the catalytic hydrogenolysis of the keto-acetate, $C_{32}H_{46}O_4$. Treatment of the acetate, $C_{32}H_{50}O_2$, with hydrochloric–acetic acid yields oleana-11 : 13(18)-dienyl acetate (X). The acetate, $C_{32}H_{50}O_2$, is not a non-conjugated dienyl acetate since, on oxidation with perbenzoic acid, it gives a product, $C_{32}H_{50}O_3$, which does not show any absorption in the ultra-violet between 2000 and 4000 Å and does not give a colour with tetranitromethane.

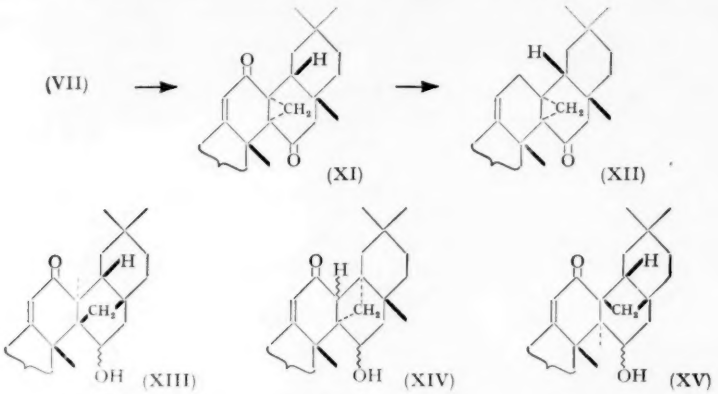
These facts lead to the conclusion that the diol monoacetate and its relatives are hexacyclic, and that notwithstanding an inherent difficulty in representing the mechanism of such a reaction, their formation from the pentacyclic *iso*oleanane derivative (I) includes the formation of a new *cyclo*alkane bridge. The transformations of the diol monoacetate and its derivatives appear at first sight to be best explained by the presence therein of a



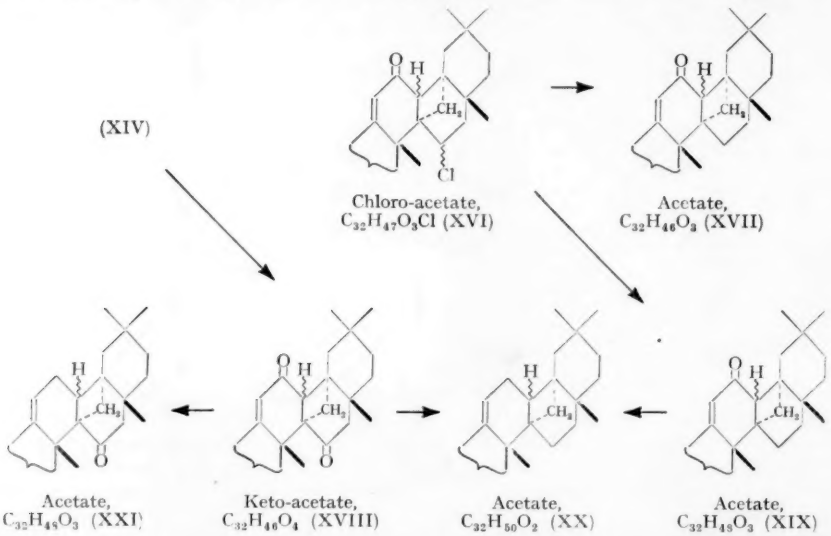
*cyclo*propane bridge. Thus the diol monoacetate may be represented by formulæ such as (VII), (VIII), and (IX), and the acetate, $C_{32}H_{50}O_2$, as (VII*a*), (VIII*a*), and (IX*a*) respectively; the acid-rearrangement of compounds of these structures to oleana-9(11) : 13(18)-dienyl acetate is adequately represented as in the annexed scheme.

Although a *cyclo*propane formulation gives a reasonable interpretation of the behaviour of the monoethenoid acetate, $C_{32}H_{50}O_2$, with mineral acid, some of the properties of this

family of compounds cannot be thus accommodated. In the first place, the infra-red absorption spectra of compounds containing a *cyclo*propane ring include an intense band at approximately 1000 cm.$^{-1}$ (Derfer, Pickett, and Boord, *J. Amer. Chem. Soc.*, 1949, **71**, 2482; Barton, *J.*, 1951, 1444): the acetate, $C_{32}H_{50}O_2$, in carbon disulphide does not show such a band. In the second place, the optical effect associated with the hyperconjugation between a *cyclo*propane ring and a carbonyl group or an ethylenic linkage (Klotz, *J. Amer. Chem. Soc.*, 1944, **66**, 88) is not observed in this series of compounds: the keto-acetate,



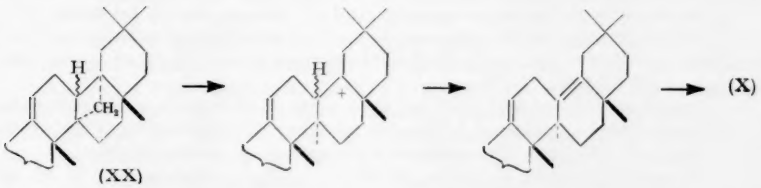
$C_{32}H_{46}O_4$, and the unsaturated acetate, $C_{32}H_{46}O_3$, show the same ultra-violet absorption characteristics as the diol monoacetate. A good illustration of this point is to be found in the following observations. Wolff–Kishner reduction of the keto-acetate, $C_{32}H_{46}O_4$, followed by acetylation, gives an acetate $C_{32}H_{48}O_3$, one of the two carbonyl groups being



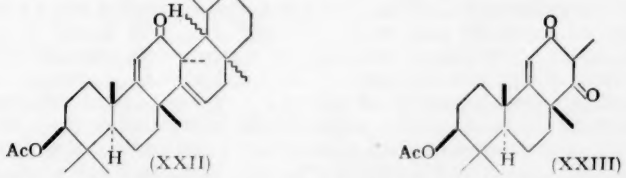
reduced to a methylene group; since the characteristic absorption spectrum of an αβ-unsaturated ketone has disappeared, the $C_{(12)}$-carbonyl group has been reduced. Consequently, if the diol monoacetate is correctly represented by one of these *cyclo*propanoid formulæ, *e.g.*, (VII), the keto-acetate will be (XI) and the Wolff–Kishner reduction product will be (XII) (or, possibly, the 11 : 12-unsaturated isomer). The ultra-violet

absorption spectrum of the Wolff–Kishner product does not show the pronounced shift towards longer wave-lengths expected for a compound containing a carbonyl group conjugated with a *cyclo*propane ring. In fact the spectrum of the Wolff–Kishner acetate, $C_{32}H_{48}O_3$, is very similar to that of the acetate, $C_{32}H_{50}O_2$, which in terms of (VII) is to be formulated as (VII*a*). For these reasons the presence of a *cyclo*propane ring in the diol monoacetate and its relatives is considered improbable and the alternative formulæ (XIII), (XIV), and (XV) are preferred for the time being. Each of these hypothetical formulæ reasonably accommodates the known reactions of the diol monoacetate. For purposes of illustration, only (XIV) will be used. Accordingly, the chloroacetate is represented by (XVI), and the compounds derived from it are (XVII)—(XXI). The conversion of (XX) into oleana-11 : 13(18)-dienyl acetate (X) is represented as shown below. The last stage in this reaction sequence, the conversion of oleana-9(11) : 13(18)-dienyl acetate into (X) has been realised (Beaton, McKean, Johnston, and Spring, *loc. cit.*).

The *cyclo*alkane bridge in the chloro-acetate (XVI), (XVII), and (XVIII) is unaffected by hydrochloric acid. This relative stability appears to be associated with the presence of a carbonyl-oxygen atom at $C_{(12)}$ and/or $C_{(15)}$: thus, the acetates (XIX) and (XX) are stable to hydrochloric–acetic acid in conditions which readily rupture the *cyclo*alkane ring of (XX).



We believe that the stability of (XIX) to mineral acid finds a counterpart in a reaction in the α-amyrin series. 12-Oxo*iso*ursa-9(11) : 14-dienyl acetate (XXII) is the α-amyrin analogue of the β-amyrin derivative, 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (I); the two acetates (XXII) and (I) are formed by parallel routes from α- and β-amyrin respectively, and each has been converted by an oxidation and pyrolytic process into the diketone (XXIII). The two acetates (XXII) and (I) differ, however, in one important



respect; whereas (I) is stable to vigorous and prolonged treatment with mineral acid, (XXII) is thereby converted into an isomer ("*iso*-α-amyradienonyl-II acetate") (Ruzicka, Ruegg, Volli, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 140) which no longer contains an isolated ethylenic linkage since, in contrast to 12-oxo*iso*ursa-9(11) : 14-dienyl acetate it does not give a colour with tetranitromethane or show the absorption at 2000—2200 Å. "*iso*-α-Amyradienonyl-II acetate" bears a very close resemblance in these and other respects to the isomeric acetate (XIX). The large change (+168°) in optical rotation associated with the conversion of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (I) into the acetate (XIX) is similar to that (+153°) accompanying the conversion of 12-oxo*iso*ursa-9(11) : 14-dienyl acetate into "*iso*-α-amyradienonyl-II acetate" {the $[\alpha]_D$ values from which this calculation was made were measured by Mr. J. D. Easton (Thesis, Glasgow University, 1953)}. We suggest that the acetate (XIX) and "*iso*-α-amyradienonyl-II acetate" have analogous structures. It is probable that the difference in behaviour of (I)

and (XXII) towards mineral acid is to be ascribed to a difference in configuration at $C_{(18)}$ and/or $C_{(17)}$ in α- and β-amyrin.

Experimental

Rotations were measured in $CHCl_3$ solution at approx. 15°. Absorption spectra were measured in alcohol solution with a Unicam SP. 500 spectrophotometer. For chromatography a grade II alumina and a light petroleum fraction, b. p. 60—80°, were used unless otherwise specified.

14 : 15-*Epoxy*-12-*oxo*iso*olean*-9(11)-*enyl Acetate*.—(*a*) A solution of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (1 g.) in dry chloroform (10 c.c.) was treated at 0° with a solution of perbenzoic acid (1·2 mols.) in chloroform (9 c.c.) and then kept at 0° for 8 days. The product crystallised from chloroform–methanol, to yield **14 : 15-*epoxy*-12-*oxo*iso*olean*-9(11)-*enyl acetate*** as plates, m. p. 280—281°, $[\alpha]_D$ −12° (*c*, 4·9) (Found : C, 77·3; H, 9·9. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%). The oxide does not give a colour with tetranitromethane. (The light absorption characteristics of this and other compounds are shown in the Table.)

(*b*) A stirred solution of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (1 g.) in acetic acid (150 c.c.) was treated dropwise with potassium permanganate (0·75 g.) in water (75 c.c.), during 30 min. After 2 hr.' stirring, the mixture was treated with 10% aqueous sodium metabisulphite, and the acetate-oxide isolated by means of ether and crystallised from methanol as rhombic plates (0·9 g.), m. p. and mixed m. p. 281—282°, $[\alpha]_D$ −12·5° (*c*, 2·1).

(*c*) 12-Oxo*iso*oleana-9(11) : 14-dienyl acetate (1·0 g.) in glacial acetic acid (80 c.c.) was treated dropwise at 60° with chromic oxide in glacial acetic acid (16 c.c., 1·5 atoms of O) during 1 hr. After 30 min.' stirring at 60°, the neutral product was isolated in the usual manner and crystallised from chloroform–methanol, to yield the acetate-oxide (0·5 g.), m. p. and mixed m. p. 280—281°, $[\alpha]_D$ −12° (*c*, 1·0).

14 : 15-*Epoxy*-12-*oxo*iso*olean*-9(11)-*enol*.—The acetate (100 mg.) was heated under reflux with 3% aqueous-ethanolic potassium hydroxide for 3 hr. Crystallisation of the product from methanol yielded **14 : 15-*epoxy*-12-*oxo*iso*olean*-9(11)-*enol*** as prismatic needles, m. p. 249·5—250°, $[\alpha]_D$ −26° (*c*, 1·4) (Found : C, 79·15; H, 10·1. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%).

Oxidation of **12-*Oxo*iso*oleana*-9(11) : 14-*dienyl Acetate with Hydrogen Peroxide : Diol Monoacetate*, $C_{32}H_{48}O_4$.**—Hydrogen peroxide (100-vol.) in acetic acid (1 : 1; 200 c.c.) was added during 2 hr. to 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (1 g.) in acetic acid (150 c.c.) at 95°. The solution was stirred for 3 hr. at 95° and the neutral product isolated in the usual manner and chromatographed in light petroleum–benzene (7 : 3; 100 c.c.) on a column (14 × 1·75 cm.) of alumina. The fractions (690 mg.) eluted with light petroleum–benzene mixtures (7 : 3, 100 c.c.; 3 : 2, 200 c.c.), benzene (300 c.c.), and benzene–ether (9 : 1; 100 c.c.) were combined and re-chromatographed in light petroleum–benzene (4 : 5; 135 c.c.) on neutral activated alumina (18 × 2 cm.). Light petroleum–benzene (4 : 5, 300 c.c.; 2 : 3, 300 c.c.; 1 : 2, 200 c.c.) eluted a crystalline solid (134 mg.), repeated crystallisation of which from chloroform–methanol yielded an *acetate* (80 mg.), m. p. 225—226°, $[\alpha]_D$ +78° (*c*, 0·7) (Found : C, 74·4, 74·7; H, 10·2, 9·5%). The acetate does not give a colour with tetranitromethane or show selective absorption of high intensity between 2200 and 4000 Å. Continued washing of the column with light petroleum–benzene (1 : 3, 100 c.c.; 1 : 4, 100 c.c.) and with benzene (250 c.c.) gave only a trace of eluate, whereafter washing with benzene–ether (9 : 1, 600 c.c.) gave a fraction (238 mg.), crystallisation of which from methanol yielded the *diol monoacetate* as plates, m. p. 318—319°, $[\alpha]_D$ +155° (*c*, 1·3) (Found : C, 77·7, 77·6; H, 9·9, 9·8. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%).

Diol, $C_{30}H_{46}O_3$.—Hydrolysis of the diol monoacetate in boiling 3% aqueous-ethanolic potassium hydroxide for 4 hr. yielded the *diol* as prisms (from aqueous methanol), m. p. 290—291°, $[\alpha]_D$ +167° (*c*, 1·0) (Found : C, 79·4; H, 10·4. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). It does not give a colour with tetranitromethane.

Diol Diacetate, $C_{34}H_{50}O_5$.—With acetic anhydride and pyridine the diol monoacetate gave the *diol diacetate*, needles from aqueous methanol, m. p. 194—194·5°, $[\alpha]_D$ +141° (*c*, 0·6) (Found : C, 75·7; H, 9·6. $C_{34}H_{50}O_5$ requires C, 75·8; H, 9·4%).

Keto-acetate, $C_{32}H_{46}O_4$.—(*a*) The diol monoacetate (120 mg.) in acetic acid (40 c.c.) was treated dropwise with chromic oxide in aqueous acetic acid (10 c.c., 1·3 atoms of O) at room temperature during 30 min. Next morning the mixture was heated on the steam-bath for 15 min., and the neutral product then isolated in the usual manner and crystallised from chloroform–methanol, to yield the *keto-acetate* as needles (80 mg.), m. p. 314—315°, $[\alpha]_D$ +94° (*c*, 1·0) (Found : C, 78·0, 77·4; H, 9·6, 9·2. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·4%).

(*b*) (i) A gently refluxing solution of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (5 g.) in glacial acetic acid (400 c.c.) was treated with chromic oxide (5 g.) in acetic acid (150 c.c.) during 1 hr. Refluxing was continued for 2 hr. and the neutral fraction isolated in the usual manner. Repeated crystallisation of this from chloroform–methanol yielded the product (1·5 g.) as needles, m. p. 315—316°, $[\alpha]_D$ +57° (*c*, 2·0). The m. p. of a mixture with the keto-acetate described under (*a*) was undepressed. A second experiment in which the crude neutral reaction product was purified by chromatography on alumina followed by crystallisation from chloroform–methanol yielded the product as needles, m. p. 313—314°, $[\alpha]_D$ +56°, +57° (*c*, 0·8, 0·3) (Found : C, 77·5, 77·4; H, 9·5, 9·2%), with an absorption maximum at 2340 Å (ε 13,000).

(ii) 14 : 15-Epoxy-12-oxo*iso*oleana-9(11)-enyl acetate (0·5 g.) in acetic acid (100 c.c.) was treated at 80° with chromic oxide (0·17 g.) in 95% acetic acid (22 c.c.), with stirring, during 4 hr. After 1 hr.' stirring the neutral product was isolated in the usual manner and crystallised from chloroform–methanol, to yield the product as needles (0·35 g.), m. p. 313—316°, $[\alpha]_D$ +58° (*c*, 1·0).

Repeated recrystallisation and careful chromatography of the neutral reaction products prepared by the two methods described under (*b*) failed to raise their rotation to that of the specimen prepared by method (*a*). It may be that the lower rotation is due to the presence of a small quantity of the acetate-oxide ($[\alpha]_D$ −12°).

Hydrolysis of the specimens of keto-acetate of low rotation for 3 hr. with boiling 3% aqueous ethanolic potassium hydroxide gave the *keto-alcohol* which, after several crystallisations from chloroform–methanol and then from methanol, separates as needles, m. p. 298—299°, $[\alpha]_D$ +71° (*c*, 0·5) (Found : C, 79·8; H, 9·9. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

The keto-alcohol was also prepared by refluxing the keto-acetate of $[\alpha]_D$ +58° (0·25 g.) in ethanol (60 c.c.) and concentrated hydrochloric acid (8 c.c.) for 3 hr. The neutral product was crystallised four times from chloroform–methanol, to yield the keto-alcohol as needles, m. p. 298—299°, $[\alpha]_D$ +71° (*c*, 0·7). A mixture with the specimen prepared by alkaline hydrolysis was undepressed in m. p. Acetylation of the keto-alcohol (pyridine–acetic anhydride) yielded the keto-acetate as needles, m. p. 313—314°, $[\alpha]_D$ +90° (*c*, 0·1), from chloroform–methanol. A mixture of this acetate with the specimen prepared by method (*a*) was undepressed in m. p.

Fission of 14 : 15-*Epoxy*-12-*oxo*iso*olean*-9(11)-*enyl Acetate with Hydrochloric Acid*: *Chloro-acetate* $C_{32}H_{47}O_3Cl$.—A solution of the oxide (1·2 g.) in chloroform (20 c.c.) and acetic acid (50 c.c.) containing concentrated hydrochloric acid (5 c.c.) was kept at 60° for 2 hr. The neutral product was isolated by means of ether and crystallised from chloroform–methanol, to yield the *chloro-acetate* as needles, m. p. 227—228° (decomp. and evolution of acidic vapour), $[\alpha]_D$ +117°, +118° (*c*, 1·3, 0·7) (Found : C, 74·8; H, 9·3; Cl, 6·5. $C_{32}H_{47}O_3Cl$ requires C, 74·6; H, 9·2; Cl, 6·9%). The chloro-acetate does not give a colour with tetranitromethane.

The chloro-acetate (150 mg.) was refluxed with potassium hydroxide (1 g.) in water (5 c.c.) and ethanol (25 c.c.) for 4 hr. The diol, $C_{30}H_{46}O_3$, isolated by means of ether in the usual manner and crystallised from aqueous methanol, formed needles, m. p. 289·5—291°, $[\alpha]_D$ +167° (*c*, 0·7). Light absorption in EtOH : Max. at 2380 Å (ε 13,500). A mixture with the diol prepared by hydrogen peroxide oxidation of 12-oxo*iso*oleana-9(11) : 14-dienyl acetate (followed by hydrolysis) was undepressed in m. p.

Treatment of the Chloro-Acetate, $C_{32}H_{47}O_3Cl$, with *Zinc* : *Acetate* $C_{32}H_{48}O_3$.—(*a*) The chloro-acetate (1 g.) in glacial acetic acid was treated with zinc (6 g.; not activated) and the mixture refluxed for 5 hr. The product was isolated by means of ether and chromatographed in light petroleum–benzene (3 : 2; 50 c.c.) on alumina (14 × 2 cm.). The fractions eluted with light petroleum–benzene (3 : 2, 550 c.c.; 2 : 3, 100 c.c.) and benzene (300 c.c.) were combined (504 mg.) and repeatedly crystallised from aqueous acetone, to give the *acetate*, $C_{32}H_{48}O_3$, as prismatic needles, m. p. 274—275°, $[\alpha]_D$ +130° (*c*, 1·4) (Found : C, 79·6; H, 10·3. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·1%). This does not give a colour with tetranitromethane in chloroform.

(*b*) The chloro-acetate (0·5 g.) in ether (75 c.c.) and methanol (75 c.c.) was treated with freshly activated zinc (5 g.) and the mixture refluxed for 5 hr. The product was isolated by means of ether, and chromatographed in light petroleum–benzene (2 : 3, 50 c.c.) on alumina (grade I) (9 × 2 cm.). The fractions eluted with light petroleum–benzene (2 : 3, 450 c.c.; 1 : 2, 300 c.c.; 1 : 5, 150 c.c.) and benzene (1000 c.c.) were combined and crystallised from aqueous acetone, to yield the acetate $C_{32}H_{48}O_3$ (400 mg.; m. p. 268—271°) which after several crystallisations from the same solvent had m. p. and mixed m. p. 273—275°, $[\alpha]_D$ +139° (*c*, 1·1). Light absorption : Max. at 2350 Å (ε 11,900).

The chloro-acetate $C_{32}H_{47}O_3Cl$ (0·25 g.) in glacial acetic acid was treated with freshly activated zinc (1·5 g.), and the mixture refluxed for 5 hr. The diol diacetate, isolated by means

of ether, crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. and mixed m. p. 197—198°, $[\alpha]_D$ +134° (*c*, 0·5) (Found : C, 75·8; H, 9·7. Calc. for $C_{34}H_{50}O_5$: C, 75·8; H, 9·4%). Light absorption : Max. at 2360 Å (ε 13,000).

Treatment of the Chloro-Acetate, $C_{32}H_{47}O_3Cl$, *with Collidine : Acetate*, $C_{32}H_{46}O_3$.—A mixture of the chloro-acetate (250 mg.) and redistilled collidine (25 c.c.) was kept at 200° in an autoclave for 3 hr. The *product* was isolated by means of ether and crystallised from chloroform–methanol as plates (180 mg.), m. p. 286—287°, $[\alpha]_D$ +117° (Found : C, 80·3; H, 9·9. $C_{32}H_{46}O_3$ requires C, 80·3; H, 9·7%). This gives a yellow colour with tetranitromethane. Light absorption : Max. at 2090 (ε 3000) and 2320 Å (ε 12,500). A solution of the acetate (30 mg.) in benzene (3 c.c.) and glacial acetic acid (10 c.c.) was treated with concentrated hydrochloric acid (0·5 c.c.) and the solution kept at room temperature for 5 days and then at 60° for 3 hr. Unchanged acetate {25 mg., m. p. 283—285°, $[\alpha]_D$ +115° (*c*, 0·5)} was recovered from the solution.

Acetate, $C_{32}H_{50}O_2$.—(a) *Catalytic hydrogenolysis of the keto-acetate*, $C_{32}H_{46}O_4$. The keto-acetate ($[\alpha]_D$ +90° ; 1·6 g.) in glacial acetic acid (250 c.c.) was added to a suspension of freshly reduced platinum (from 0·5 g. of PtO_2) in glacial acetic acid (20 c.c.), and the mixture shaken with hydrogen for 48 hr. The filtered solution was shaken with fresh platinum catalyst (from 0·25 g. of PtO_2) for 24 hr. and the product isolated in the usual manner. The product was chromatographed in light petroleum–benzene (2 : 1; 150 c.c.) on alumina (grade II/III; 14 × 2 cm.). Light petroleum–benzene (2 : 1, 400 c.c.) eluted a fraction (1·34 g.) which was repeatedly crystallised, first from methanol–ether and then from methanol–chloroform, to yield (with considerable loss) the *acetate*, $C_{32}H_{50}O_2$, as hexagonal plates, m. p. 231—232°, $[\alpha]_D$ +86°, +87° (*c*, 1·0, 1·5) (Found : C, 82·5; H, 10·8. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). Light absorption : $\varepsilon_{2080} = 3000$, $\varepsilon_{2100} = 2800$, $\varepsilon_{2150} = 1800$, $\varepsilon_{2200} = 860$.

The earlier mother-liquors obtained from the crystallisation of the foregoing acetate were combined and concentrated, to give needles, m. p. 164—166° (0·6 g.). Four crystallisations of these from methanol yielded an *acetate*, $C_{32}H_{52}O_2$, as needles, m. p. 168—170°, $[\alpha]_D$ +12°, +13° (*c*, 1·3) (Found : C, 81·95; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Light absorption : $\varepsilon_{2060} = 1520$, $\varepsilon_{2100} = 1000$, $\varepsilon_{2150} = 650$, $\varepsilon_{2250} = 280$.

(b) *Wolff–Kishner reduction of the acetate*, $C_{32}H_{48}O_3$. A mixture of the acetate, $C_{32}H_{48}O_3$ (obtained by reduction of the chloro-acetate, $C_{32}H_{47}O_3Cl$, with zinc) (0·5 g.), methanolic sodium methoxide (from 2 g. of sodium and 25 c.c. of methanol), and hydrazine hydrate (100% ; 5 c.c.) was kept at 200° in an autoclave for 10 hr. The product was isolated in the usual manner and acetylated with pyridine and acetic anhydride. A solution of the acetylated product in light petroleum (50 c.c.) was chromatographed on alumina (14 × 2 cm.). The fractions eluted with light petroleum (500 c.c.) were combined (240 mg.) and crystallised from chloroform–methanol, to give the acetate, $C_{32}H_{50}O_2$, as plates, m. p. 226—228°, $[\alpha]_D$ +84° (*c*, 1·0), undepressed in m. p. when mixed with the specimen prepared by method (a). Light absorption : $\varepsilon_{2100} = 2600$, $\varepsilon_{2150} = 2000$, $\varepsilon_{2200} = 850$. A second experiment gave the same acetate as plates (from chloroform–methanol), m. p. 230—231°, $[\alpha]_D$ +86°.

Oleana-11 : 13(18)-*dienyl Acetate from the Acetate*, $C_{32}H_{50}O_2$.—The acetate, $C_{32}H_{52}O_2$ (65 mg.), in acetic acid (35 c.c.) was heated with concentrated hydrochloric acid (3 c.c.) on the steam-bath for 5 hr. and then kept overnight at room temperature. The product was isolated by means of ether, acetylated (warm pyridine–acetic anhydride), and crystallised from chloroform–methanol, to yield oleana-11 : 13(18)-dienyl acetate (38 mg.) as plates, m. p. and mixed m. p. 226—228°, $[\alpha]_D$ −61° (*c*, 0·7). Light absorption : Max. at 2430 (ε 26,000), 2510 (ε 28,000) and 2600 Å (ε 20,000).

Treatment of the Acetate, $C_{32}H_{50}O_2$, *with Perbenzoic Acid*.—The acetate, $C_{32}H_{50}O_2$ (340 mg.), in chloroform (25 c.c.) was treated at 0° with perbenzoic acid (210 mg.) in chloroform (2 c.c.) and then kept at 0° for 4 days. Crystallisation from chloroform–methanol gave, as first crop, unchanged acetate $C_{32}H_{50}O_2$ (100 mg.), m. p. 219—223°, m. p. and mixed m. p. 225—227°, $[\alpha]_D$ +81° (*c*, 1·5), on recrystallisation. The original chloroform–methanol mother-liquor was concentrated to give a second crop (110 mg.), recrystallisation of which from the same solvent mixture yielded the *oxide* as plates, m. p. 194—195°, $[\alpha]_D$ +23° (*c*, 1·0) (Found : C, 79·4; H, 10·7. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). The oxide does not give a colour with tetranitromethane or show selective absorption between 2000 and 4000 Å.

Wolff–Kishner Reduction of the Keto-acetate, $C_{32}H_{46}O_4$.—The acetate $C_{32}H_{46}O_4$ (m. p. 313—314°, $[\alpha]_D$ +90° ; 1 g.), methanolic sodium methoxide (from 30 c.c. of methanol and 2·5 g. of sodium), and hydrazine hydrate (100% ; 10 c.c.) were heated at 200° in an autoclave for 16 hr. The product was isolated by means of ether, acetylated (acetic anhydride–pyridine at 80°),

dried, and chromatographed in light petroleum (50 c.c.) on grade II—III alumina (14 × 2 cm.). Elution with light petroleum–benzene mixtures gave a solid (500 mg.), crystallisation of which from methanol yielded the *acetate* as plates, m. p. 227—229°, $[\alpha]_D$ −2·5°, −2° (*c*, 2·0, 2·8) (Found: C, 79·6; H, 10·1. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·1%). Light absorption: $\varepsilon_{2090} = 3400$, $\varepsilon_{2150} = 2000$, $\varepsilon_{2200} = 1100$. The acetate gives a yellow colour with tetranitromethane and was recovered unchanged after 3 hr.' warming of 50 mg. on the water-bath with glacial acetic acid (25 c.c.) and concentrated hydrochloric acid (3·5 c.c.).

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Tetrazolium Compounds. Part II. Azo-derivatives.*

By D. D. LIBMAN, A. W. NINEHAM, and R. SLACK.

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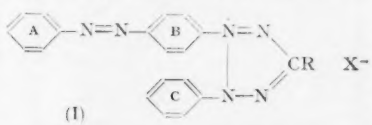
A new series of formazans and corresponding tetrazolium salts is described. In each compound, an *N*-phenyl group bears a phenylazo-substituent.

IN Part I* of this series, some tetrazolium salts bearing three variously substituted benzene rings were described. Of these, 3-*p*-aminophenyl-2 : 5-diphenyltetrazolium chloride showed slight activity in laboratory experiments against influenza A and Nigg mouse pneumonitis viruses,† and was chosen as a model for further study, the amino-group being replaced by phenylazo, to give (I) (R = Ph) (formal localisation of the charge on $N_{(2)}$ is not to be construed literally). The present communication deals with the preparation of substituted derivatives of (I) which could behave as biological precursors of the simpler amino-compounds. Effects of substitution in the benzene rings have been examined and two bis-tetrazolium salts have been prepared (polymethylene bridge at R).



(I)

The general synthetic methods employed are described in Part I.* Complete diazotisation of some aminoazo-compounds was difficult and was best performed in glacial acetic acid with nitrosylsulphuric acid or with sulphuric acid and a paste of sodium nitrite in water. This involved the use of larger volumes of pyridine to neutralise the excess of acid during condensations with the phenylhydrazones, but the virtual absence of water led to purer products.

Variants of ring A were introduced by the use of aminoazo-compounds prepared by (i) coupling *p*-acetamidobenzenediazonium chloride with substituted benzene derivatives, (ii) coupling diazonium salts with sodium *N*-methylaniline-ω-sulphonate, or (iii) rearrangement of diazoamino-compounds in the presence of aniline hydrochloride. Variations in ring B were obtained by application of the above methods to α-naphthylamine and *p*-xylidine. Variations in R were achieved by the use of different aldehydes and in ring C by the use of substituted phenylhydrazines.

The azoformazans did not differ markedly from the compounds described in Part I, but were a more intense purple or black and were less soluble in organic solvents. This was especially true of hydroxy-compounds. Purification was not difficult but combustion analyses for nitrogen were not always satisfactory.

Oxidations were sometimes slow but the only failures were with 1 : 3-diphenyl-5-(4-*p*-acetamidophenylazophenyl)- and 1 : 3-diphenyl-5-(4-*p*-dimethylaminophenylazophenyl)-

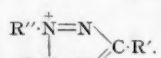
* Part I, *J.*, 1953, 3881.

† We thank Dr. R. Wien and Mr. W. F. Freeman for drawing our attention to this property of some of the tetrazolium salts described in this series of papers. Detailed biological results will be published elsewhere by our colleagues.

TABLE 1. *Formazans*, R·NH·N:CR′·N:NR″.

No.	R	R′	R″	Yield (%)	Appearance	M. p.	Solvent
1 [a]	Ph	Ph	*p*-C_6H_4·N:NPh	50	Purplish-black	182° *	Aq. $COMe_2$
2 [a]	Ph	Me	,,	28	Dark red	115	,,
3	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4Me-*p*	53	Black, purplish-red reflex [d]	186—188	EtOAc
4	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4Cl-*p*	11·5	Dark purple [d]	194·5—195	,,
5	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4·NO_2-*p*	57	Purplish-black, golden reflex [e]	205—206 *	$CHCl_3$
6	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4·OH-*p*	28	Dark purple, red reflex [d]	198—200	Me·NO_2
7	Ph	Ph	*p*-C_6H_4·N:N·C_6H_3Cl·OH-1 : 2 : 4	27	Dark purple, yellow reflex [f]	149—150	,,
8	Ph	Ph	*p*-C_6H_4·N:N·C_6H_3Cl·OH-1 : 3 : 4	8	Black, greenish-golden reflex	205—210	,,
9	Ph	Ph	4-Phenylazo-1-naphthyl	9 [b]	Indigo-blue [d]	200	$CHCl_3$
10	Ph	*p*-C_6H_4·OH	*p*-C_6H_4·N:NPh	50	Dark purple [d]	180	MeOH
11	Ph	Ph	2 : 5 : 4-$C_6H_2Me_2$·N:NPh	50	Dark purple, green reflex [d]	197 *	EtOAc
12	*p*-C_6H_4·CO_2H	Ph	*p*-C_6H_4·N:NPh	10	Black, green reflex [f]	209	,,
13 [a]	*p*-C_6H_4Cl	Ph	,,	18	Purplish-black	168—170	Aq. $COMe_2$
14 [a]	*p*-C_6H_4·NHAc	Ph	,,	26	Purple	215	,,
15 [c]	Ph	$-[CH_2]_2-$	,,	29	Purple	136—138	*cyclo*Hexane
16 [c]	Ph	$-[CH_2]_6-$	,,	39	Purplish-black [e]	161—162 *	C_6H_6–*cyclo*hexane
17	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4·NHAc-*p*	35	Dark red [e]	216	$CHCl_3$–MeOH
18	Ph	Ph	*p*-C_6H_4·N:N·C_6H_4·NMe_2-*p*	23	Dark purple	182	Me·NO_2
19	*p*-C_6H_4·NHAc	*p*-C_6H_4·NHAc	*p*-C_6H_4·N:N·C_6H_4·OH-*p*	small	Dark purple	188	MeOH
20	Ph	Ph	2 : 5-Dimethyl-4-2′-thiazolylazo-phenyl	25	Violet [d]	216 *	$CHCl_3$
21	Ph	*p*-C_6H_4·OAc	*p*-C_6H_4·N:NPh	50	Dark purple [d]	191	EtOAc

[a] Prepared by (Miss) B. M. Davies. [b] Overall yield from aniline and α-naphthylamine. [c] This is the bis-compound. [d] Needles. [e] Prisms. [f] Plates. * With decomp.

TABLE 2. *Tetrazolium salts*,  .

No.*	Yield (%)	Anion	Method of oxidn.	Appearance	M. p. †	Solvent
1	24	I	B	Orange	231—232°	MeOH
2	—	I	B	Orange needles	127—129	EtOH–Et_2O
3	36	I	A	Ruby-red prisms	175—177	EtOH
4	72	Cl	A	Red needles	184—185	EtOH–Et_2O
5	45	Cl	B	Orange-red prisms	250	Aq. EtOH
6	70	Cl	C	Orange-red prisms	230	EtOH–Et_2O
7	26	Cl	C	Dark red prisms	204—205	,,
8	53	Cl	C	Dark orange-red prisms	206—207	,,
9	48	I	B	Orange needles	280	Aq. EtOH
10	97	Cl	C	Orange-brown rhombs	267	EtOH
11	54	Cl	A	Orange prisms	41	H_2O
12	48	Cl	A	Red prisms	264	MeOH
13	33	I	B	Orange	219	MeOH–Et_2O
14	40	I	B	Orange	258	EtOH–Et_2O
15	69	I	B	Dark red	185—186	EtOH
16	24	I	A	Red prisms	169—170	,,

Methods of oxidation: A, Mercuric oxide in methanol; B, lead tetra-acetate in chloroform; C, *iso*amyl nitrite and hydrogen chloride.

* The tetrazolium salts have the R, R′, and R″ of the formazans of corresponding number in Table 1. † With decomp., except no. 13.

formazan. In these cases undesirable secondary oxidations can occur. Most of the tetrazolium salts were sparingly soluble in water. The isethionates, into which some iodides were converted, were not markedly more soluble than the halides. The new salts and the corresponding formazans are listed in Tables 1 and 2.

Experimental

p-*Acetoxybenzaldehyde phenylhydrazone* formed triangular plates (from ethanol) (95%), m. p. 154° (Found: N, 10·7. $C_{15}H_{14}O_2N_2$ requires N, 11·0%).

p-*Acetamidobenzaldehyde* p-*Acetamidophenylhydrazone*.—*p*-Acetamidophenylhydrazine stannichloride (Franzen and von Fürst, *Annalen*, 1916, **412**, 41) (100 g., 0·2 mol.) and crystalline sodium acetate (100 g.) in hot water (1 l.) were heated with a solution of *p*-acetamidobenzaldehyde (33 g., 0·2 mol.) in aqueous methanol at 95° for 30 min., to give the *phenylhydrazone* as cream-coloured needles (40%), m. p. 233° (from aqueous methanol) (Found: N, 18·3. $C_{17}H_{18}O_2N_4$ requires N, 18·1%).

Table 3. *Analyses of formazans.*

		Found (%)				Required (%)			
No.*	Formula	C	H	N	Cl	C	H	N	Cl
1	$C_{25}H_{20}N_6$	74·2	5·3	20·0	—	74·3	5·0	20·8	—
2	$C_{20}H_{18}N_6,H_2O$	66·9	5·6	23·1	—	66·7	5·6	23·3	—
3	$C_{26}H_{22}N_6$	74·3	5·0	—	—	74·6	5·3	—	—
4	$C_{25}H_{19}N_6Cl$	—	—	18·9	7·8	—	—	19·1	8·1
5	$C_{25}H_{19}O_2N_7$	67·0	4·2	21·5	—	66·8	4·2	21·8	—
6	$C_{25}H_{20}ON_6$	70·4	5·0	19·4	—	71·4	4·8	20·0	—
7	$C_{25}H_{19}ON_6Cl$	—	—	17·9	7·0	—	—	18·5	7·8
8	$C_{25}H_{19}ON_6Cl$	—	—	—	7·1	—	—	—	7·8
9	$C_{29}H_{22}N_6$	—	—	18·4	—	—	—	18·5	—
10	$C_{25}H_{20}ON_6,\frac{1}{2}CH_3{\cdot}OH$	70·6	5·0	18·6	—	70·2	5·0	19·3	—
11	$C_{27}H_{24}N_6$	75·2	5·6	19·1	—	75·0	5·6	19·4	—
12	$C_{26}H_{20}O_2N_6$	69·7	5·2	18·2	—	69·6	4·5	18·7	—
13	$C_{25}H_{19}N_6Cl$	68·7	4·5	—	8·0	68·5	4·3	—	8·1
14	$C_{27}H_{23}ON_7$	70·2	4·9	—	—	70·2	5·0	—	—
15	$C_{40}H_{34}N_{12}$	70·5	5·2	23·1	—	70·5	5·0	24·6	—
16	$C_{44}H_{42}N_{12},C_6H_{12}$	72·1	6·3	20·5	—	71·9	6·5	20·4	—
17	$C_{27}H_{23}ON_7$	69·7	5·0	20·9	—	70·2	5·0	21·2	—
18	$C_{27}H_{25}N_7$	72·2	5·7	21·2	—	72·5	5·6	21·9	—
19	$C_{29}H_{26}O_3N_8,2CH_3{\cdot}OH$	62·0	5·2	—	—	62·0	5·0	—	—
20	$C_{24}H_{21}N_7S$	—	—	21·6	6·8 †	—	—	22·3	7·3 †
21	$C_{27}H_{22}O_2N_6$	70·5	5·0	17·8	—	70·1	4·8	18·2	—

* Cf. Table 1. † Sulphur analysis.

Table 4. *Analyses of tetrazolium salts.*

		Found (%)				Required (%)			
No.*	Formula	C	H	N	Hal.	C	H	N	Hal.
1	$C_{25}H_{19}N_6I$	56·4	3·6	—	23·9	56·5	3·6	—	24·0
2	$C_{20}H_{17}N_6I$	51·2	4·1	—	27·0	51·3	3·6	—	27·1
3	$C_{26}H_{21}N_6I$	56·0	3·8	15·7	23·9	57·4	3·8	15·4	23·3
4	$C_{25}H_{18}N_6Cl_2,1{\cdot}5H_2O$	60·3	4·4	16·8	14·2	60·0	4·2	16·8	14·2
5	$C_{25}H_{18}O_2N_7Cl,2H_2O$	57·8	4·5	19·0	6·7	57·8	4·2	18·8	6·8
6	$C_{25}H_{19}ON_6Cl,\frac{1}{2}H_2O$	64·6	4·3	17·9	7·5	64·7	4·3	18·1	7·6
7	$C_{25}H_{18}ON_6Cl_2,H_2O$	59·5	4·1	16·2	13·7	59·2	3·6	16·6	14·0
8	$C_{25}H_{18}ON_6Cl_2,C_2H_5{\cdot}OH$	60·2	4·7	15·8	13·0	60·5	4·5	15·7	13·2
9	$C_{29}H_{21}N_6I$	—	—	14·2	22·0	—	—	14·5	21·9
10	$C_{25}H_{19}ON_6Cl$	—	—	19·0	7·4	—	—	18·5	7·8
11	$C_{27}H_{23}N_6Cl,3H_2O$	—	—	16·3	6·8	—	—	16·2	6·8
12	$C_{26}H_{19}O_3N_6Cl,\frac{1}{2}H_2O$	63·2	4·2	16·6	6·8	63·4	4·1	17·0	7·0
13	$C_{25}H_{18}N_6ClI$	52·8	3·4	—	22·4 †	53·1	3·2	—	22·5 †
14	$C_{27}H_{22}ON_7I$	55·0	3·8	—	21·6	55·1	3·8	—	21·6
15	$C_{40}H_{32}N_{12}I_2,C_2H_5{\cdot}OH$	—	—	16·5	25·8	—	—	17·1	25·9
16	$C_{44}H_{40}N_{12}I_2,H_2O$	—	—	16·7	25·3	—	—	16·7	25·3

* Cf. Table 2. † Iodine analysis.

4-p-*Aminophenylazo*-2-*chlorophenol*.—Diazotised *p*-acetamidoaniline was coupled with *o*-chlorophenol. Hydrolysis with hydrochloric acid gave the *aminoazo*-compound (51%), m. p.

186—187° (from aqueous ethanol) (Found: C, 58·7; H, 4·3; N, 17·2. $C_{12}H_{10}O_3NCl$ requires C, 58·2; H, 4·3; N, 16·9%).

4-p-*Aminophenylazo-3-chlorophenol*, prepared in the same way, formed orange plates (83%), m. p. 165°, from aqueous ethanol (Found: N, 15·8; Cl, 13·6. $C_{12}H_{10}ON_3Cl,H_2O$ requires N, 15·8; Cl, 13·4%). The N-*acetyl* derivative, golden needles (from ethanol), had m. p. 213—215° (Found: N, 14·2. $C_{14}H_{12}O_2N_3Cl$ requires N, 14·5%).

2-p-*Aminophenylazothiazole*.—Diazotised 2-aminothiazole was coupled with sodium *N*-methylaniline-ω-sulphonate in alkaline solution (cf. Elbs, *J. pr. Chem.*, 1924, [2], **108**, 229). Hydrolysis of the intermediate sulphonate with hot 50% sodium hydroxide solution gave the *aminoazo*-compound (36%), dark red rhombs or stout prisms, m. p. 188—189° (from toluene) (Found: N, 27·3. $C_9H_8N_4S$ requires N, 27·5%). The N-*acetyl* compound, m. p. 231°, formed orange needles (88%) from 50% ethanol (Found: N, 22·0. $C_{11}H_{10}ON_4S$ requires N, 22·8%).

2 : 5-*Dimethyl-4-2′-thiazolylazoaniline* was obtained as dark red prisms with a green reflex (from benzene) or as crimson needles [from benzene–light petroleum (b. p. 60—80°) (1 : 1)], m. p. 158° (28%) (Found: C, 57·8; H, 5·2; N, 23·0; S, 14·0. $C_{11}H_{12}N_4S$ requires C, 57·0; H, 5·2; N, 24·1; S, 13·8%). The N-*acetyl* derivative formed orange prisms or yellow needles, m. p. 187° (from benzene) (Found: N, 20·2; S, 12·1. $C_{13}H_{14}ON_4S$ requires N, 20·3; S, 11·6%).

4-2′-*Thiazolylazo-1-naphthylamine* formed purple needles (from 60% ethanol), m. p. 195° (60%) (Found: N, 21·5. $C_{13}H_{10}N_4S$ requires N, 22·0%). The N-*acetyl* derivative formed brown needles (60%), m. p. 236° (from ethanol) (Found: N, 18·8. $C_{15}H_{12}ON_4S$ requires N, 18·9%).

The following formazans were not isolated from the appropriate condensations: 1 : 3-diphenyl-5-*p*-(*p*-sulphophenylazo)phenyl-, 5-(4-*p*-hydroxyphenylazo-1-naphthyl)-1 : 3-diphenyl-, 3-*p*-acetoxyphenyl-5-*p*-(4-hydroxyphenylazo)phenyl-1-phenyl-, 1 : 3-diphenyl-5-(4-2′-thiazolylazophenyl)-, 5-[2 : 5-dichloro-4-(2 : 5-dichlorophenylazo)phenyl]-1 : 3-diphenyl-, 1 : 3-diphenyl-5-(1-phenylazo-2-naphthyl)-, 1 : 3-diphenyl-5-(4-1′-naphthylazo-1-naphthyl)-, 1 : 3-diphenyl-5-(4-2′-thiazolylazo-1-naphthyl)-, and 1-*p*-nitrophenyl-3-phenyl-5-*p*-phenylazophenyl-formazan, octamethylenebis-3-(1-phenyl-5-*p*-phenylazophenylformazan) and octamethylenebis-3-(1-*p*-nitrophenyl-5-*p*-phenylazophenylformazan).

We thank Dr. A. J. Ewins, F.R.S., for his interest, Mr. S. Bance, B.Sc., and his staff for semi-microanalyses, and the Directors of May & Baker Ltd. for permission to publish these results.

Research Laboratories, May & Baker Ltd.,
Dagenham, Essex. [*Received, December 30th*, 1953.]

Tetrazolium Compounds. Part III. Styryl Derivatives.*

By A. W. Nineham, D. L. Pain, and R. Slack.

[Reprint Order No. 5027.]

The preparation of a number of 1 : 3-disubstituted 5-styrylphenylformazans † and of the corresponding tetrazolium salts is described.

Part II * of this series described the preparation and properties of tetrazolium salts in which benzene rings attached to the tetrazolium nucleus carried phenylazo-substituents. The present paper describes a similar series of salts in which the attached benzene rings bear styryl, or in a few cases, both styryl and phenylazo-groups. The compounds were prepared in order to examine the effect of extended conjugation on the colour of the formazans and on the biological activity of the tetrazolium salts. 2 : 5-Diphenyl-3-*p*-styrylphenyltetrazolium chloride has been used by Henley (Ann. Report, Dept. Rheumatic Diseases, W. London Hospital, 1952, p. 24) for the colorimetric estimation of small amounts of cortisone.

Most of the intermediates required are known substances. 4-Amino-4′-hydroxy- (Brownlee, Copp, Duffin, and Tonkin, *Biochem. J.*, 1943, **37**, 572) and 4-acetamido-4′-aminostilbene (Brode and Piper, *J. Amer. Chem. Soc.*, 1941, **63**, 1502) were prepared by

* Part II, preceding paper. † See Part I, *J.*, 1953, 3881, for nomenclature of formazans.

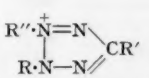
iron-dust reductions of the corresponding nitro-compounds and Cullinane's method (*J.*, 1923, **123**, 2056) was applied to the preparation of 4-bromo-4'-nitrostilbene (l'Ecuyer, Giguère, Olivier, and Roberge, *Canad. J. Res.*, 1948, **26**, *B*, 70). 4-Amino-4'-bromostilbene (mentioned but not described by Thompson, Vago, Corfield, and Orr, *J.*, 1950, 214) was obtained from this by reduction with stannous chloride.

TABLE 1. *Formazans*, R·NH·N:CR'·N:NR''.

	R	R'	R''	Yield (%)	M. p.	Appearance	Solvent
1	Ph	Me	*p*-C_6H_4·CH:CHPh	68	160—162°	Dark orange [a]	A
2	Ph	Me	*p*-C_6H_4·CH:CH·C_6H_4·NO_2-*p*	16	182—183	Dark orange [a]	B
3	Ph	Ph	*p*-C_6H_4·CH:CHPh	74	185	Purple, green reflex [b]	C
4	Ph	*p*-C_6H_4·OMe	,,	83	157—158	Purple [a]	D
5	Ph	*p*-C_6H_4Br	,,	47	170—171	Purple [b]	D
6	Ph	Ph	*p*-C_6H_4·CH:CH·C_6H_4·NO_2-*p*	33	185—186	Purple, golden reflex [b]	E
7	Ph	Ph	*p*-C_6H_4·CH:CH·C_6H_4Br-*p*	33	186—187	Purple [c]	E
8	Ph	Ph	*p*-C_6H_4·CH:CH·C_6H_4·OH-*p*	32	175—176	Purple [d]	B
9	Ph	Ph	*p*-C_6H_4·CH:CH·C_6H_4·NHAc-*p*	14	208—209	Purple, green reflex [b]	B
10	*p*-C_6H_4·N:NPh	Ph	*p*-C_6H_4·CH:CHPh	47	*	Purplish black, red reflex	D
11	,,	*p*-C_6H_4·CO_2H	,,	33	239—240	Black	F
12	,,	*p*-C_6H_4·OAc	,,	40	220—221	Purple [d]	E
13	Ph	Me	*p*-C_6H_4·CH:CH·C_6H_4·NHAc-*p*	12	203	Red [d]	G

A, Ethanol; B, nitromethane; C, ethyl acetate; *D*, *cyclo*hexane; *E*, benzene; F, acetone; G, nitroethane.

* Not obtained analytically pure. [a] Plates. [b] Needles. [c] Rods. [d] Prisms.

TABLE 2. *Tetrazolium salts*, 

No.*	Anion	Method of oxidn.	Yield (%)	M. p.	Appearance	Solvent
1	I	(i)	34	169—172°	Yellow needles	A
2	I	(i)	28	222—223	Yellow	B
3a	Cl	(i)	54	228	Yellow needles	C
3b	Isethionate	—	37	181	Yellow prisms	B
3c	$\frac{1}{2}SO_4$	—	86	†	Yellow	B
3d	HSO_4	—	71	169—171	Yellow needles	D
4	I	(i)	39	167—168 †	,,	E
5	I	(i)	14	206 †	,,	F
6	Cl	(i)	57	233—234	Pale yellow prisms	B
7	Cl	(i)	67	216—217	Yellow needles	B
8	I	(i)	25	272 †	Orange rods	A
9	I	(i)	41	244 †	Orange rectangular plates	E
10	I	(i)	20	175 † (sinters 151—152)	Orange-red	E
11	Cl	(ii)	11	195 †	Red	E
12	Cl	(ii)	58	215—216 †	Red rods	G

* The tetrazolium salts have the R, R', and R'' of the formazans of corresponding number in Table 1. † With decomp. (i) Mercuric oxide; (ii) *iso*amyl nitrite. Solvents: A, methanol; B, ethanol–ether; C, water; D, 0·5N-sulphuric acid; E, ethanol; F, acetone–methanol–light petroleum (b. p. 60—80°); G, acetone–ether, containing a trace of methanol.

The formazans (see Tables 1 and 3) were prepared by methods already described in Parts I and II. Except for 5-*p*-(4-acetamidostyryl)phenyl-3-methyl-1-phenylformazan, all the formazans were satisfactorily oxidised to tetrazolium salts (see Tables 2 and 4) by standard methods.

Experimental

4-Amino-4′-hydroxystilbene.—4-Hydroxy-4′-nitrostilbene (Cullinane, *loc. cit.*) (11·0 g.) and iron pin-dust (11·0 g.) in Cellosolve (2-ethoxyethanol) (120 c.c.) were heated to 90°, concentrated hydrochloric acid (6 c.c.) in water (3 c.c.) was added slowly, and the suspension stirred vigorously

Table 3. *Analyses of formazans.*

No.*	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
1	$C_{22}H_{20}N_4$	—	—	16·3	—	—	16·5
2	$C_{22}H_{19}O_3N_5$	68·4	5·0	17·7	68·5	4·9	18·2
3	$C_{27}H_{22}N_4$	80·4	5·8	13·6	80·6	5·5	13·9
4	$C_{28}H_{24}ON_4$	77·7	5·7	—	77·8	5·6	—
5	$C_{27}H_{21}N_4Br$	—	—	11·6	—	—	11·6
6	$C_{27}H_{21}O_2N_5$	72·4	4·9	—	72·4	4·7	—
7	$C_{27}H_{21}N_4Br$	—	—	11·6	—	—	11·6
8	$C_{27}H_{22}ON_4,\frac{1}{2}H_2O$	76·5	5·5	12·9	75·9	5·4	13·1
9	$C_{29}H_{25}ON_5$	75·8	5·5	15·4	75·7	5·5	15·2
11	$C_{34}H_{26}O_2N_6$	74·3	5·0	—	74·2	4·8	—
12	$C_{35}H_{28}O_2N_6$	74·4	5·1	14·5	74·5	5·0	14·9
13	$C_{24}H_{23}ON_5$	72·2	6·0	17·3	72·5	5·8	17·6

* Cf. Table 1.

Table 4. *Analyses of tetrazolium salts.*

No.*	Formula	Found (%) C	Found (%) H	Found (%) N	Found (%) Hal.	Found (%) S	Required (%) C	Required (%) H	Required (%) N	Required (%) Hal.	Required (%) S
1	$C_{22}H_{19}N_4I,\frac{1}{2}H_2O$	—	—	11·8	26·6	—	—	—	11·8	26·7	—
2	$C_{22}H_{18}O_2N_5I$	—	—	13·7	24·6	—	—	—	13·7	24·8	—
3a	$C_{27}H_{21}N_4Cl,H_2O$	—	—	12·3	7·9	—	—	—	12·3	7·8	—
3b	$C_{29}H_{26}O_4N_4S$	—	—	10·9	—	6·2	—	—	10·7	—	6·1
3c	$C_{54}H_{42}O_4N_8S,2H_2O$	—	—	11·9	—	3·4	—	—	12·0	—	3·4
3d	$C_{27}H_{22}O_4N_4S$	—	—	11·9	—	6·5	—	—	11·2	—	6·4
4	$C_{28}H_{23}ON_4I$	—	—	10·1	22·8	—	—	—	10·0	22·8	—
5	$C_{27}H_{20}N_4BrI$	—	—	9·4	70·9 †	—	—	—	9·2	69·8 †	—
6	$C_{27}H_{20}O_2N_5Cl,2H_2O$	—	—	13·5	6·7	—	—	—	13·5	6·8	—
7	$C_{27}H_{20}N_4ClBr,H_2O$	—	—	10·4	63·0 †	—	—	—	10·5	62·1 †	—
8	$C_{27}H_{21}ON_4I$	—	—	10·6	23·3	—	—	—	10·3	23·4	—
9	$C_{29}H_{24}ON_5I,H_2O$	58·0	4·2	11·4	21·7	—	57·7	4·3	11·6	21·1	—
10	$C_{33}H_{25}N_6I$	—	—	12·7	20·7	—	—	—	13·3	20·1	—
11	$C_{34}H_{25}O_2N_6Cl,H_2O$	67·5	4·3	—	6·3	—	67·8	4·5	—	5·9	—
12	$C_{33}H_{45}ON_6Cl,4H_2O$	63·5	4·3	13·4	—	—	63·0	5·2	13·4	—	—

* Cf. Table 2. † Total silver halide.

for 4 hr. The mixture was cooled, neutralised with sodium carbonate (6 g.), and diluted with water to give the amine (62%).

4-Amino-4′-bromostilbene.—4-Bromo-4′-nitrostilbene was reduced with stannous chloride and hydrogen chloride in acetic acid. The stannichloride was decomposed with aqueous 50% sodium hydroxide, and the crude product was extracted from the residue with acetone and crystallised from *sec.*-butanol, to give the *amino-stilbene* (65%) as orange plates, m. p. 203—205° (Found: N, 5·3; Br, 29·0. $C_{14}H_{12}NBr$ requires N, 5·1; Br, 29·2%).

4-Acetamido-4′-aminostilbene.—4-Acetamido-4′-nitrostilbene (Ashley *et al.*, *J.*, 1942, 103) was reduced with iron dust in boiling 90% acetic acid, to give the aminostilbene (92%), m. p. 235° (from anisole).

Preparation of 4-Phenylazophenylhydrazones.—Aldehydes were condensed with *N*-4-phenylazophenylhydrazine-*N*′-sulphonic acid by Träger, Berlin, and Franke's method (*Arch. Pharm.*, 1906, **244**, 307, 326), to give p-*acetamido*-, brick-red prisms (from ethanol), m. p. 190—191° (Found: C, 67·7; H, 5·8; N, 18·4. $C_{21}H_{19}ON_5,H_2O$ requires C, 67·2; H, 5·7; N, 18·6%), p-*hydroxy*-, lustrous orange plates (from benzene), m. p. 208—209° (Found: C, 73·1; H, 5·1; N, 17·3. $C_{19}H_{16}ON_4$ requires C, 72·1; H, 5·1; N, 17·7%), p-*acetoxy*-, small orange prisms (from ethanol), m. p. 161—162° (Found: N, 15·6. $C_{21}H_{18}O_2N_4$ requires N, 15·6%), and the *ammonium* salt of p-*carboxybenzylidene-4-phenylazophenylhydrazine*, yellow powder (from ethanol), m. p. 245° (Found: C, 66·3; H, 5·0; N, 19·0. $C_{20}H_{19}O_2N_5$ requires C, 66·5; H, 5·3; N, 19·4%).

Tetrazolium Salts.—Tetrazolium chlorides were converted into the sulphates by treatment

with the calculated amount of silver sulphate in boiling water. Addition of dilute sulphuric acid gave the corresponding hydrogen sulphates. The isethionate was obtained by passing a solution of the chloride in aqueous ethanol through a column of " Amberlite IRA 400 (OH^-) " ion-exchange resin and neutralising the filtrate with isethionic acid.

The following could not be isolated : 5-*p*-(4-bromostyryl)phenyl-3-methyl-1-phenyl-, 5-*p*-(4-hydroxystyryl)phenyl-3-methyl-1-phenyl-, 3-(2 : 4-dichlorophenyl)-1-phenyl-5-*p*-styrylphenyl-, 1-phenyl-3-styryl-5-*p*-styrylphenyl-, 3-*p*-hydroxyphenyl-1-*p*-phenylazophenyl-5-*p*-styrylphenyl- and 3-*p*-acetamidophenyl-1-*p*-phenylazophenyl-5-*p*-styrylphenyl-formazan.

We thank Mr. S. Bance, B.Sc., A.R.I.C., for the semi-microanalyses, Dr. A. J. Ewins, F.R.S., for his interest, and the Directors of May & Baker Ltd. for permission to publish the results.

RESEARCH LABORATORIES, MAY & BAKER LTD., DAGENHAM. [*Received, January 13th,* 1954.]

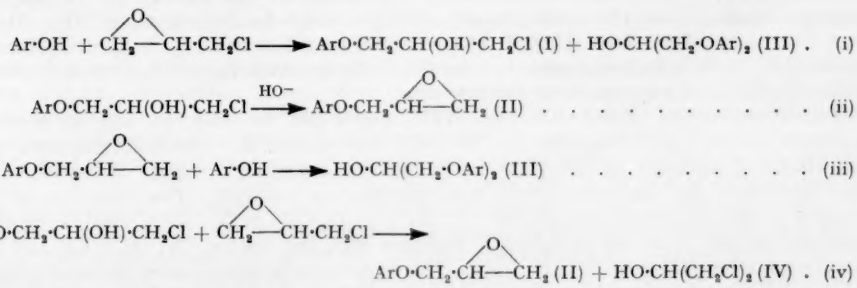
The Condensation of Epichlorohydrin with Monohydric Phenols and with Catechol.

By O. STEPHENSON.

[Reprint Order No. 5043.]

The method described earlier (*J.*, 1951, 1589) for the preparation of 1-aryloxy-3-chloropropan-2-ols has been improved to give increased yields. The condensation of catechol with epichlorohydrin in the presence of basic catalysts has been investigated and the hitherto unknown bisglycide ether (VIII) obtained.

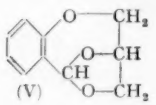
THE preparation of 1-aryloxy-3-chloropropan-2-ols (I) by condensation of phenols with epichlorohydrin in the presence of basic catalysts (cf. i) has been described by Bradley, Forrest, and Stephenson (*J.*, 1951, 1589). The method, however, is not entirely satisfactory as optimum yields of products are only obtained by leaving reaction mixtures at room temperature for periods exceeding one month. For this reason and because of the increasing importance of the products as intermediates, their preparation has been studied further and an improved procedure developed.


Ar·OH + CH₂—CH·CH₂Cl → ArO·CH₂·CH(OH)·CH₂Cl (I) + HO·CH(CH₂·OAr)₂ (III) . (i)
ArO·CH₂·CH(OH)·CH₂Cl —HO⁻→ ArO·CH₂·CH—CH₂ (II) . . . . . (ii)
ArO·CH₂·CH—CH₂ + Ar·OH → HO·CH(CH₂·OAr)₂ (III) . . . . . (iii)
ArO·CH₂·CH(OH)·CH₂Cl + CH₂—CH·CH₂Cl →
ArO·CH₂·CH—CH₂ (II) + HO·CH(CH₂Cl)₂ (IV) . (iv)

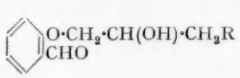
It was already known that phenols and epichlorohydrin in equimolar amounts in the presence of a basic catalyst give an aryloxychlorohydrin (I) [reaction (i)] in 50—70% yield, together with smaller quantites of the glyceryl αα′-diaryl ether (III); the latter is also obtained by way of the aryl glycide ether (II) [reactions (ii) and (iii)]. Further study of reaction (i) revealed that formation of (III) is virtually suppressed by employing excess of epichlorohydrin. When the chlorohydrin (I) is heated with 3 mols. of epichlorohydrin and a suitable basic catalyst for some hours on the water-bath, glycerol dichlorohydrin (IV) and an equivalent amount of aryl glycide ether (II), together with unchanged chlorohydrin (I), are obtained [cf. (iv); Bradley *et al., loc. cit.*]. The foregoing experiments showed clearly that reaction of phenols with excess of epichlorohydrin leads to the formation of (I), (II), and (IV) with exclusion of (III). A basis for an improved route to aryloxychlorohydrins (I) was thus presented as the glycide (II) was known to pass into the

chlorohydrin with great facility on treatment with hydrochloric acid. The procedure finally adopted is given on p. 1573.

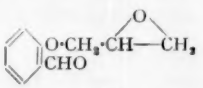
An attempt to extend this reaction to salicylaldehyde gave much polymeric material, a crystalline product $C_{10}H_{10}O_3$, and a small quantity of the desired ether (VI; R = Cl). The last compound with sodium hydroxide at room temperature gave the glycide ether (VII), which reacted smoothly with piperazine and *p*-chlorophenol.



(V)

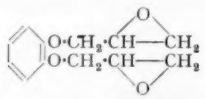


(VI)

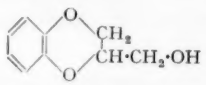


(VII)

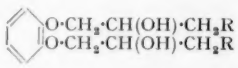
The structure (V) is assigned to the product $C_{10}H_{10}O_3$, on the following evidence: (i) The compound does not possess a free aldehyde group as it fails to react with hydroxylamine or semicarbazide under the usual experimental conditions; (ii) the ultra-violet absorption spectrum fails to reveal a carbonyl group associated with an aromatic nucleus; (iii) no free hydroxyl or alkali-sensitive groups are present as the material is recovered unchanged after treatment with alkali, phenyl *iso*cyanate, or boiling acetic anhydride; and (iv) with dinitrophenylhydrazine in ethanolic mineral acid it gives a dinitrophenylhydrazone identical with that from authentic (VI; R = OH), which is conveniently prepared from salicylaldehyde and glycidol.



(VIII)



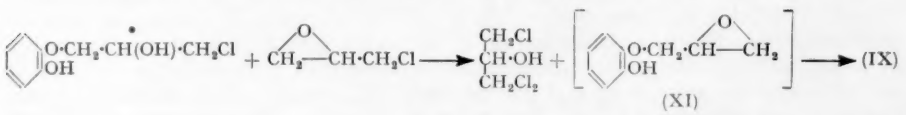
(IX)



(X)

The bisglycidyl ethers of resorcinol and quinol have been prepared by Werner and Farenhorst (*Rec. Trav. chim.*, 1948, **67**, 438) by reaction of the dihydric phenols with epichlorohydrin in aqueous alkaline solution, but attempts to obtain the corresponding catechol derivative (VIII) have not hitherto been successful. Thus Lindemann (*Ber.*, 1891, **24**, 2149) heated catechol with two equivalents of epichlorohydrin in aqueous potassium hydroxide at 120° and obtained a product which he claimed was (VIII). However, Fourneau (*Chem. Zent.*, 1910, I, 1134) showed that this was 2-hydroxymethylbenzodioxen (IX); this is indistinguishable from (VIII) by analysis, but is found to differ from authentic (VIII) now obtained for the first time.

Direct conversion of catechol into (VIII) could not be achieved, but an indirect approach *via* the bischlorohydrin (X; R = Cl) was successful. The last compound was first obtained, although in low yield, by condensing equivalent weights of catechol and epichlorohydrin on the steam-bath, with pyridine as catalyst. Fractionation of the product yielded the monochlorohydrin (I; Ar = C_6H_4·OH) in 35—45% yield, somewhat increased by use of excess of catechol, together with the diether (X; R = Cl) and the biscatechol ether (III; Ar = C_6H_4·OH). The monochlorohydrin yielded the benzodioxen (IX), *o*-(3-amino-2-hydroxypropyl)phenol, and *o*-(2-hydroxy-3-piperidinopropyl)phenol on treatment with an alkaline reagent, ammonia solution, and piperidine, respectively. Reaction with ammonia also yielded appreciable amounts of the benzodioxen by intramolecular reaction from the intermediate monoglycide ether (XI). Attempts to improve



(XI)

the yield of diether (X; R = Cl) by increasing the proportion of epichlorohydrin proved only partly successful: using two equivalents and heating the mixture for *ca.* 6 hr. on the water-bath gave a 20% yield of (X; R = Cl); the benzodioxen (IX) was the major product, being

evidently formed by interaction of the monochlorohydrin with excess of epichlorohydrin as indicated. Employing four mols. of epichlorohydrin in the presence of piperidine hydrochloride and leaving the mixture for *ca.* 40 days at room temperature, however, completely suppressed this reaction and the diether (X; R = Cl) was obtained in 74% yield. Heating this reaction mixture at *ca.* 95° for 10 hr. gave the benzodioxen and smaller quantities of epoxides and chlorohydrins of unestablished structure. In one experiment catechol was condensed with epichlorohydrin (2·2 mols.) in the presence of concentrated aqueous sodium hydroxide for 12 days at room temperature, yielding a mixture of the mono- and di-ethers without formation of high-boiling products. It seems certain therefore that with a larger excess of epichlorohydrin this reaction could be adapted to give an optimum yield of diether (X; R = Cl).

Careful reaction of the diether (X; R = Cl) with alkali gave the required bisglycide ether (VIII) as a liquid of b. p. 132—140°/0·2 mm. which slowly crystallised, leaving an oily residue which may have contained a stereoisomer (cf. Werner and Farenhorst, *loc. cit.*).

Experimental

The following illustrates the general method for preparation of the aryloxychlorohydrins (I). The phenol is heated with 3 mols. of epichlorohydrin for 4—6 hr. at *ca.* 100° in the presence of a catalytic quantity of piperidine or other base (see below). After removal of excess of epichlorohydrin by distillation under reduced pressure on the water-bath, the residue is cooled, dissolved in an equal volume of chloroform, and shaken with excess of concentrated hydrochloric acid to convert glycide ether into chlorohydrin. The whole is then washed with water to remove excess of acid and glycerol dichlorohydrin, the solvent is removed at reduced pressure, and the residue distilled *in vacuo*. Pyridine, piperidine, piperidine acetate, or piperidine hydrochloride is about equally effective as catalyst. Piperidine (2 ml./mole of phenol) was employed for convenience. The yields obtained were uniformly 70—85% (see Table 1).

Reaction between 1-*Chloro*-3-p-*methoxyphenoxypropan*-2-*ol and Epichlorohydrin.*—A solution of 1-chloro-3-*p*-methoxyphenoxypropan-2-ol (54·1 g.) in epichlorohydrin (69·4 g.) containing pyridine (0·5 ml.) was heated at 95° for 10 hr., after which excess of epichlorohydrin was removed under reduced pressure. Fractionation of the residue under reduced pressure yielded unchanged aryloxychlorohydrin, crude glycerol dichlorohydrin (6·8 g.) and a fraction (12 g.) of b. p. *ca.* 150°/15 mm. Refractionation of the latter oil gave a solid (6 g.) which on crystallisation from ether formed colourless prisms of glycide *p*-methoxyphenyl ether, m. p. and mixed m. p. 48° (Found: C, 66·8; H, 6·6. Calc. for $C_{10}H_{12}O_3$: C, 66·6; H, 6·7%).

Condensation of Salicylaldehyde with Epichlorohydrin.—Salicylaldehyde (122 g.), epichlorohydrin (278 g.), and pyridine (4 ml.) were heated on the steam-bath for 6 hr., slight initial cooling being applied to keep the temperature below 110°. The excess of epichlorohydrin was removed at reduced pressure and the residue fractionated *in vacuo* to yield: (i) 60 g., b. p. 48—56°/0·5 mm., which on redistillation at atmospheric pressure yielded glycerol dichlorohydrin (40·2 g.), b. p. 174—178°, (ii) 70 g., b. p. 110—130°/0·5 mm., and (iii) 66 g., b. p. 180°/0·5 mm., of crude chlorohydrin. Distillation was stopped at this point as the residue had begun to decompose. Fraction (ii) was purified by crystallisation from ether–light petroleum (b. p. 40—60°), forming white needles (47·6 g.) of the acetal, 4 : 7-*epoxy*-2 : 3-*benzo*-1 : 5-*dioxa*cyclo*octene* (V), m. p. 65° (Found: C, 67·5; H, 5·6. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%). This formed a 2 : 4-*dinitrophenylhydrazone* (in alcoholic mineral acid) which separated from ethanol in sparingly soluble orange-red needles, m. p. 208—209° (Found: C, 51·3; H, 4·3; N, 15·3. $C_{16}H_{16}O_7N_4$ requires C, 51·1; H, 4·3; N, 14·9%). Fraction (iii) on redistillation yielded a main fraction, b. p. 164°/0·1 mm., of o-(3-*chloro*-2-*hydroxypropyl*)*benzaldehyde* (Found: C, 56·5; H, 5·2; Cl, 15·7. $C_{10}H_{11}O_3Cl$ requires C, 55·9; H, 5·2; Cl, 16·5%). The 2 : 4-*dinitrophenylhydrazone* separated from alcoholic hydrochloric acid in dark-red plates, m. p. 188° (Found: C, 48·2; H, 3·8; N, 14·4; Cl, 8·7. $C_{16}H_{15}O_6N_4Cl$ requires C, 48·7; H, 3·8; N, 14·1; Cl, 9·0%).

Condensation of Salicylaldehyde with Glycidol.—To a mixture of salicylaldehyde (24·4 g.) and glycidol (14·8 g.) was added pyridine (5 drops) and the solution heated on the steam-bath for 5 hr. o-(2 : 3-*Dihydroxypropyl*)*benzaldehyde* (23 g.) separated on cooling. After crystallisation from ethyl acetate–light petroleum (b. p. 60—80°), it formed light yellow needles, m. p. 85° (Found: C, 61·3; H, 6·1. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·2%). The 2 : 4-*dinitrophenylhydrazone*, prepared in acetic acid, formed orange crystals, m. p. 206—208° (Found: C, 50·8;

H, 4·1; N, 14·6. $C_{16}H_{16}O_7N_4$ requires C, 51·1; H, 4·3; N, 14·9%), not depressed on admixture with the material prepared from (V).

Conversion of o-(3-*Chloro*-2-*hydroxypropyl*)*benzaldehyde into Glycidyl* o-*Formylphenyl Ether* (VII).—The crude chlorohydrin (VI; R = Cl) was stirred vigorously for 3 hr. with N-sodium hydroxide. The product was extracted with chloroform, the extract washed and concentrated,

TABLE 1. *Yields of* 1-*aryloxy*-3-*chloropropan*-2-*ols.*

No.	Ar	Mols. of epichlorohydrin per mol. of phenol	Catalyst *	Catalyst (g./mole of phenol)	Yield (%) of (I)
1	Phenyl	1·5	B	2	63
		3·0	C	2	78
2	*o*-Tolyl	1·5	B	2	56
		,,	,,	4	53
		,,	,,	8	56
		,,	C	2	55
		,,	,,	4	55
		3·0	,,	2	75
		,,	A	2	81
3	*m*-Tolyl	1·5	B	2	61
		3·0	C	2	80
4	*p*-Tolyl	1·5	B	2	61
		3·0	C	2	90
5	*o*-Methoxyphenyl	1·05	B	1	34
		,,	,,	2	50
		1·5	,,	2	56
		,,	,,	4	62
		3·0	C	2	82
6	*m*-Methoxyphenyl	1·05	B	1	37
		1·5	,,	2	62
		3·0	C	2	81
7	*p*-Methoxyphenyl	1·05	B	1	40
		,,	A	1	41
		1·5	B	2	60
		3·0	C	2	76
8	*o*-Chlorophenyl	1·5	B	2	75
		,,	,,	4	72
		,,	NH_4Cl	2	67
		,,	C	2	73
		3·0	,,	2	84
9	*p*-Chlorophenyl	1·5	B	2	71
		3·0	C	2	85
		,,	,,	2	87
10	*o*-Bromophenyl	3·0	C	2	89
11	*p*-Bromophenyl	3·0	A	2	81
12	o-*Iodophenyl*	3·0	A	2	76
13	o-*Nitrophenyl*	1·5	B	2	69
		3·0	,,	8	73
		,,	A	2	76
14	m-*Nitrophenyl*	3·0	A	2	76
15	*p*-Nitrophenyl	1·5	B	2	59
		3·0	A	2	83
16	2 : 4 : 6-Tribromophenyl	3·0	C	2	68
17	2 : 4-Dichlorophenyl	3·0	B	2	82
18	p-*Cyanophenyl*	3·0	A	3	80
19	o-*Formylphenyl*	3·0	D	2	*ca.* 18
20	p-*Formylphenyl*	3·0	C	1	68
21	p-*Ethoxycarbonylphenyl*	3·0	C	4	77
22	α-Naphthyl	3·0	A	2	85
23	β-Naphthyl	3·0	A	2	78
24	Thymyl	3·0	A	2	65
25	Carvacryl	3·0	A	2	68
26	4-Chloro-3-methylphenyl	3·0	A	2	86
27	2 : 6-*Dichloro*-4-*ethoxycarbonylphenyl*	6·0	D	1·5	73

* A = Piperidine. B = Piperidine acetate. C = Piperidine hydrochloride. D = Pyridine.

and the resultant oil distilled *in vacuo*, yielding o-(2 : 3-*epoxypropyl*)*benzaldehyde* (VII), b. p. 118°/0·5 mm. (Found: C, 67·2; H, 5·9. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%).

Reactions. (i) The glycide ether (11·3 g.) was treated with piperazine hexahydrate (6·2 g.) in ethanol (10 ml.), an exothermic reaction occurring, after which it was left overnight. Dilution with water yielded a gum which was converted into the hydrochloride which separated from

90% ethanol in small white crystals, m. p. 236—237° (decomp.), of 1 : 4-*di*-(3-o-*formylphenoxy*-2-*hydroxypropyl*)*piperazine dihydrochloride* (Found : C, 56·0; H, 6·3; N, 5·2; Cl, 13·5. $C_{24}H_{32}O_6N_2Cl_2$ requires C, 55·9; H, 6·3; N, 5·4; Cl, 13·8%).

(ii) The glycide ether (6·05 g.) and *p*-chlorophenol (4·4 g.) were melted together, pyridine (2 drops) was added, and the mixture heated on the steam-bath for 6 hr. The resultant gum solidified on trituration with dilute aqueous sodium hydroxide and separated from aqueous methanol in pale-yellow prisms of 1-p-*chlorophenoxy*-3-o-*formylphenoxypropan*-2-*ol*, m. p. 97—99° (Found : C, 62·7; H, 5·0; Cl, 11·8. $C_{16}H_{15}O_4Cl$ requires C, 62·6; H, 4·9; Cl, 11·6%).

Condensation of p-*Hydroxybenzaldehyde with Epichlorohydrin.*—This yielded 1-chloro-3-*p*-formylphenoxypropan-2-ol which formed a 2 : 4-*dinitrophenylhydrazone* in alcoholic hydrochloric acid. This separated from glacial acetic acid in small, dark-red shining plates, m. p. 209—212° (Found : N, 14·5; Cl, 9·4. $C_{16}H_{15}O_6N_4Cl$ requires N, 14·1; Cl, 9·0%).

TABLE 2. 1-*Aryloxy*-3-*chloropropan*-2-*ols* (I).

No.	B. p. (°/mm.)	n_D^{20}	Formula	Required (%) C	H	Cl	Found (%) C	H	Cl
1	178/15	1·5413	$C_9H_{11}O_2Cl$	57·9	6·0	19·0	58·5	6·4	18·5
2	104/0·3	1·5363					59·7	6·5	17·2
3	200/30—35	1·5360	$C_{10}H_{13}O_2Cl$	59·8	6·5	17·7	—	—	17·6
4	192/20	1·5349					60·2	6·5	17·4
5	194/15	—					55·2	6·2	16·6
6	144/0·5	1·5431	$C_{10}H_{13}O_3Cl$	55·4	6·1	16·4	55·6	6·1	16·3
7	200/15	1·5413					55·8	6·1	16·4
8	200/20	1·5518	$C_9H_{10}O_2Cl_2$	48·8	4·6	32·1	49·5	4·6	31·5
9	216/30	1·5540					49·4	4·5	—
10	128/0·3	—	$C_9H_{10}O_2ClBr$	40·6	3·8	43·5 *	41·1	4·3	42·5 *
11	138/0·3	1·5723					40·8	3·8	44·1 *
12	130/0·1	—	$C_9H_{10}O_2ClI$	34·6	3·2	52·0 *	35·1	3·4	51·2 *
13	160/0·5	1·5650	$C_9H_{10}O_4NCl$ [a]	46·6	4·4	15·3	46·5	4·5	15·4 *
15	176/0·2	1·5900					46·9	4·4	15·3
16	172/0·1	—	$C_9H_8O_2ClBr_2$	25·5	1·9	65·1 *	26·3	2·3	64·8 *
17	148/0·6	1·5641	$C_9H_9O_2Cl_3$	42·3	3·5	41·7	42·4	3·5	—
18	166/0·3	—	$C_{10}H_{10}O_2NCl$ [b]	56·7	4·8	16·8	56·9	4·6	—
19	164/0·1	—	$C_{10}H_{11}O_3Cl$	55·9	5·2	16·5	56·5	5·2	15·7
20	178/0·3	—					56·3	5·5	16·2
21	158/0·1	—	$C_{12}H_{15}O_4Cl$	55·7	5·9	13·7	55·3	5·6	13·6
22	158/0·1	—	$C_{13}H_{13}O_2Cl$	65·9	5·5	15·0	65·4	5·5	15·5
23	174/0·2	—					66·4	5·4	—
24	106/0·1	1·5231	$C_{13}H_{19}O_2Cl$	64·3	7·9	14·6	64·7	7·8	14·3
25	120/0·1	1·5222					—	—	14·4
26	136/0·5	—	$C_{10}H_{12}O_2Cl_2$	51·0	5·2	30·2	51·1	5·3	30·1
27	190/1·0	—	$C_{12}H_{13}O_4Cl_3$	44·0	4·0	32·5	44·6	3·9	31·7

* Total halogen. [a] Found : N, 6·3 (no. 13), 6·0 (no. 15). Reqd. : N, 6·1%. [b] Found : N, 6·2. Reqd. : N, 6·6%.

Condensation of Catechol with Epichlorohydrin.—(i) *With* 1 *mol. of epichlorohydrin.* (a) To a hot solution of catechol (110 g.) in epichlorohydrin (92·5 g.), pyridine (1 ml.) was added and the solution heated on the steam-bath for 2 hr., with cooling to keep the temperature below 105°. The mixture was distilled directly *in vacuo*, yielding the following fractions : (*a*) 13·5 g. of crude glycerol dichlorohydrin, b. p. <70°/0·2 mm., (*b*) 20 g. of unchanged catechol, b. p. 80—90°/0·1—0·2 mm., (*c*) 97·5 g., b. p. 120—140°/0·1—0·3 mm., (*d*) 31·5 g., b. p. 180°/0·2—0·3 mm., and (*e*) 10 g., b. p. >220°/0·2—0·5 mm. The residue was beginning to decompose.

Fraction (*c*) solidified and crystallised from ethyl acetate–light petroleum (b. p. 60—80°), yielding white needles of o-(3-*chloro*-2-*hydroxypropyl*)*phenol*, m. p. 88—90° (Found : C, 53·6; H, 5·6; Cl, 17·7. $C_9H_{11}O_2Cl$ requires C, 53·3; H, 5·5; Cl, 17·5%). This (10·1 g.) was refluxed in water (50 ml.) containing potassium carbonate (6·9 g.) for 4 hr. After cooling, the oil was extracted with chloroform, and the extract washed, concentrated, and diluted with light petroleum (b. p. 60—80°), yielding 5-hydroxymethylbenzodioxen (5·7 g.), m. p. 86—92°, not depressed on admixture with an authentic specimen (see below). Acetylation of the chlorohydrin (20 g.) with acetic anhydride (50 ml.) under reflux for 2 hr. yielded the *diacetyl* derivative (20 g.), b. p. 138—140°/0·25 mm. (Found : Cl, 12·1. $C_{13}H_{15}O_5Cl$ requires Cl, 12·4%).

Fraction (*d*) consisted mainly of the bischlorohydrin (X; R = Cl) (see below).

Fraction (*e*) set to a glass which crystallised on remelting. After recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) and then from aqueous methanol, 1 : 3-*di*-o-

hydroxyphenoxypropan-2-ol was obtained as plates, m. p. 172° (Found: C, 65·0; H, 5·7. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%).

(b) In a similar experiment the reaction product was dissolved in chloroform, shaken with concentrated hydrochloric acid, and washed with much water to remove excess of catechol. After working up as before a 36% yield of the pure monochlorohydrin, b. p. 140°/0·2 mm., was obtained.

(ii) *With 0·86 mol. of epichlorohydrin.* A mixture of catechol (2·45 mol.), epichlorohydrin (2 mol.), and piperidine acetate (2 g.) was heated at 95° for 6 hr. (initial cooling to keep the temperature below 115°). Treatment as in (i,a) yielded (*a*) 184 g. (46%) of pure monochlorohydrin, b. p. 140°/0·2 mm., (*b*) 18 g. of (X; R = Cl), b. p. 180°/0·2 mm., and (*c*) 70 g., b. p. >220°/0·2 mm., which yielded (III; Ar = C_6H_4·OH) (18 g.) and non-crystalline complex products which were not investigated further.

(iii) *With 2 mols. of epichlorohydrin.* A mixture of catechol (33 g.) and epichlorohydrin (55·5 g.) containing pyridine (0·5 ml.) was heated on the steam-bath for 4 hr. (max. temp. 103°). Low-boiling material was removed at reduced pressure and the residue distilled *in vacuo*, yielding (*a*) 26 g. (50%), b. p. 120°/0·1 mm., and (*b*) 20 g. (23%), b. p. 186°/0·1 mm. Fraction (*a*) crystallised from ethyl acetate–light petroleum (b. p. 60—80°) and then from benzene–light petroleum (b. p. 40—60°), yielding 2-hydroxymethylbenzodioxen in white prismatic needles, m. p. 90—92° (Found: C, 65·2; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·0; H, 6·1%), m. p. strongly depressed on admixture with the monochlorohydrin. Fraction (*b*), on redistillation, had b. p. 166°/0·05 mm. Crystallisation from benzene–light petroleum (b. p. 60—80°) and then from ether–light petroleum (b. p. 40—60°) yielded o-*di*-(3-*chloro*-2-*hydroxypropyl*)*benzene* (X; R = Cl) in needles, m. p. 79° (Found: Cl, 23·8. $C_{12}H_{16}O_4Cl_2$ requires Cl, 24·1%). When this was stirred vigorously for 30 min. with a slight excess of aqueous-alcoholic potassium hydroxide it was converted into o-*di*-(2 : 3-*epoxypropyl*)*benzene*, obtained after two distillations *in vacuo* as an oil, b. p. 132—140°/0·2 mm. (Found: C, 64·6; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·8; H, 6·4%). The oil solidified gradually and then crystallised from ether–light petroleum (b. p. 40—60°) as needles, m. p. 44—46°. This ether (6·7 g.) was condensed with *n*-butylamine (5·25 g.) by warm benzene–light petroleum (b. p. 60—80°), giving o-(3-n-*butylamino*-2-*hydroxypropyl*)*benzene*, needles (from ethyl acetate), m. p. 120° (Found: C, 64·9; H, 9·7; N, 8·2. $C_{20}H_{36}O_4N_2$ requires C, 65·2; H, 9·9; N, 7·6%).

(iv) *With 4 mols. of epichlorohydrin.* (a) When a solution of catechol (55 g.) in epichlorohydrin (185 g.) containing piperidine hydrochloride (0·5 g.) was left at room temperature for 39 days and the product distilled *in vacuo*, the diether (X; R = Cl) was obtained in 74% yield, b. p. 180°/0·1 mm.

(b) The mixture used in the preceding example was heated on the steam-bath for 20 hr. After removal of excess of epichlorohydrin at reduced pressure, distillation of the residue *in vacuo* yielded the benzodioxen (43 g., 52%), b. p. 126—128°/0·5 mm., m. p. 90—92° [from benzene–light petroleum (b. p. 40—60°)], a complex mixture of epoxides and chlorohydrins (20·2 g.), b. p. 164°/0·5 mm., and the diether (X; R = Cl) (15·5 g.), b. p. 194°/0·5 mm.

(v) *With 2·2 mols. of epichlorohydrin, and sodium hydroxide as catalyst.* A solution of catechol (55 g.) in epichlorohydrin (102 g.) was treated with sodium hydroxide (0·5 g.) dissolved in a few drops of water, and the mixture left in an atmosphere of nitrogen for 12 days. After washing and concentration at reduced pressure, the resultant residue was distilled *in vacuo*, yielding the monochlorohydrin (34·4 g., 34%), b. p. 164°/0·5 mm., identified by conversion into (IX), and the bischlorohydrin (71·7 g., 49%), b. p. 194°/0·5 mm., m. p. and mixed m. p. 78—79° after crystallisation as previously.

Reaction of o-(3-*Chloro*-2-*hydroxypropyl*)*phenol with Bases.*—A solution of the chlorohydrin (15 g.) in ethanol (50 ml.) was treated with aqueous ammonia (*d* 0·880; 60 ml.) and the solution refluxed gently for 3 hr., then concentrated at reduced pressure. Water (50 ml.) was added and the mixture extracted with chloroform (3 × 50 ml.). The aqueous extract was acidified with concentrated hydrochloric acid (25 ml.) and evaporated on the steam-bath. The pink crystalline material which separated (6 g.; m. p. *ca.* 168°) was collected and washed with cold ethanol. Repeated crystallisation from ethanol–light petroleum (b. p. 60—80°) yielded needles of o-(3-*amino*-2-*hydroxypropyl*)*phenol hydrochloride*, m. p. 177—180° (Found: C, 48·9; H, 6·2; N, 6·5; Cl, 16·2. $C_9H_{14}O_3NCl$ requires C, 49·2; H, 6·4; N, 6·4; Cl, 16·2%). The original chloroform extract was washed, concentrated to *ca.* 25 ml., and diluted with light petroleum (b. p. 60—80°). The solids which separated (6 g.) were purified by crystallisation from benzene–light petroleum (b. p. 40—60°), to give needles of the benzodioxen (IX), m. p. and mixed m. p. 90—92°.

A solution of the monochlorohydrin (10·1 g.) and piperidine (12·75 g.) in ethanol (20 ml.) was

refluxed for 8 hr. After concentration at reduced pressure the gummy residue was converted into the hydrochloride. Crystallisation from methanol–ethyl acetate gave o-(2-*hydroxy*-3-*piperidinopropyl*)*phenol hydrochloride* (6·5 g.) as fawn-coloured needles (Found: N, 4·7; Cl, 12·5. $C_{14}H_{22}O_3NCl$ requires N, 4·9; Cl, 12·3%).

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Molecular Polarisability. Its Anisotropy in Aliphatic and Aromatic Structures.

By (MRS.) C. G. LE FÈVRE and R. J. W. LE FÈVRE.

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The use of depolarisation factors in the analysis of molecular polarisability is criticised on practical grounds, and an alternative information source is proposed. New determinations of the molar Kerr constants at infinite dilution are recorded for 26 substances, and the semi-axes of their optical polarisability ellipsoids calculated. Comparisons of data for structures related as alphyl–X and aryl–X suggest that exaltation of polarisability occurs preferentially in those directions for which electromeric shifts are, from organo-chemical theory, expected to be easiest. Anisotropic polarisabilities of bonds are considered incidentally, and signs detected of inductomeric polarisability effects in the *tert.*-butyl group. Results are generally in harmony with conclusions reached by Ingold in a recent monograph.

THE work described in this paper was started with the intention of comparing the anisotropic polarisabilities of structures related as alphyl–X and aryl–X. We have previously dealt with the determination of "molar Kerr constants" ($_mK_2$) of solutes and their extrapolation to infinite dilution (*J.*, 1953, 4041); by the same methods, new measurements have now been completed on 26 compounds, thus making available knowledge of $_\infty(_mK_2)$ for each of the molecules listed in Table 1. All except nitromethane and 1 : 3 : 5-trinitrobenzene have been examined in carbon tetrachloride.

TABLE 1. *Molar Kerr constants * at infinite dilution.*

Temp.	Solute	$_\infty(_mK_2) \times 10^{12}$	Temp.	Solute	$_\infty(_mK_2) \times 10^{12}$
20°	CH_3F	28·3 ± 3	25°	C_6H_5Br	171 ± 3
25	CH_3Cl	32·3 ± 2	20	C_6H_5I	186 ± 1·5
25	CH_3Br	51·6 ± 0·7	20	$C_6H_5{\cdot}NO_2$ ‡	1073 ± 14
25	CH_3I	54·2 ± 2	20	$C_6H_5{\cdot}CN$	1147 ± 35
25	$CH_3{\cdot}NO_2$ †	89·0 ± 3	20	1 : 2-$C_6H_4Me_2$	25·1$_5$ ± 0·3
25	$CH_3{\cdot}CN$	219·5 ± 6	20	1 : 3-$C_6H_4Me_2$	13·0 ± 0·2
25	$(CH_3)_3CCl$	85·6 ± 3	25	1 : 4-$C_6H_4Me_2$	10·6 ± 0·5
25	$(CH_3)_3CBr$	146 ± 4	20	1 : 4-$C_6H_4Cl_2$	38·6 ± 2
25	$(CH_3)_3CI$	203 ± 6	20	1 : 4-$C_6H_4Br_2$	40·3 ± 2
25	C_2Cl_6	4·60 ± 0·8	20	1 : 3 : 5-$C_6H_3Me_3$	10·1 ± 0·3
20	C_6H_6	7·24 ± 0·4	20	1 : 3 : 5-$C_6H_3Cl_3$	37·6 ± 1
25	C_6H_5Me	12·8 ± 0·2$_5$	20	1 : 3 : 5-$C_6H_3Br_3$	24·3 ± 2
20	C_6H_5F	56·8 ± 0·8	25	1 : 3 : 5-$C_6H_3(NO_3)_3$ †	168 ± 12
20	C_6H_5Cl ‡	145 ± 1·5	25	C_6Me_6	16·0 ± 1
			20°	C_6Cl_6	103·6 ± 0·3

* With estimated standard errors.
† Examined in benzene.
‡ Data recalculated from *J.*, 1953, 4041.

Before proceeding to our primary objective we need to consider two matters: (*a*) the deduction from $_\infty(_mK_2)$ and other experimental quantities of estimates of molecular polarisability ellipsoids, and (*b*) the calculation of bond polarisabilities.

(a) *Calculation of Molecular Polarisability Ellipsoids.*—The problem, in the general case, is to find the principal half-axes, b_1, b_2, and b_3, of the ellipsoid of polarisability for a given molecule. Three equations are therefore necessary. The first of these involves ${}_mK_2$:

$$ {}_mK_2 = 2\pi N(\theta_1 + \theta_2)/9 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1) $$

The second is derived from the electronic polarisation:

$$ {}_EP = 4\pi N(b_1 + b_2 + b_3)/9 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2) $$

The third expresses the depolarisation factor Δ of scattered light in terms of the required half-axes:

$$ 10\Delta/(6 - 7\Delta) = [(b_1 - b_2)^2 + (b_2 - b_3)^2 + (b_3 - b_1)^2]/(b_1 + b_2 + b_3)^2 \quad . \quad (3) $$

In (1), θ_1 and θ_2 may be expanded as shown by the relations Nos. (13) and (14) in our previous paper. In particular, θ_1 becomes

$$ \theta_1 = ({}_DP/45\boldsymbol{k}T \,.\, {}_EP)[(b_1 - b_2)^2 + (b_2 - b_3)^2 + (b_3 - b_1)^2] \quad . \quad . \quad (4) $$

If therefore ${}_mK_2$, ${}_EP$, the distortion polarisation ${}_DP$, $\mu_{\text{resultant}}$ (and its direction of action with respect to the polarisability ellipsoid), and Δ are known for a substance, b_1, b_2, and b_3 can be computed.

Unfortunately, however, depolarisation factors are available only for a few dozen molecules (Cabannes, " La Diffusion Moléculaire de la Lumière," Les Presses Universitaires de France, 1929, lists 61) of fairly simple type. Moreover, Δ is markedly affected by state, so that for the purposes of equation (3) one requires " la dépolarisation limite " (Cabannes, *op. cit.*, pp. 38, 105), *i.e.*, Δ for the scattering from a gas " assez voisin de l'état parfait." Recorded values for the same substance are not always in agreement with one another.

In a limited number of cases Δ can be checked, since for structures having, by symmetry, $b_1 = b_2$ or $b_2 = b_3$, half-axes may be computed without recourse to Δ. Table 4 contains 15 instances where this has been done. The b's so obtained can be used to estimate the numerator of the right-hand side of (3), and the result compared with the figure deduced *via* $2\delta_0^2 = 10\Delta/(6 - 7\Delta)$. An analysis of the five cases for which the requisite depolarisation factors have been reported is shown as Table 2. For brevity, A is written for $(b_1 - b_2)^2 + (b_2 - b_3)^2 + (b_3 - b_1)^2$. Table 2 includes also the magnitudes of θ_1, for two unsymmetrical molecules, obtained from $2\delta_0^2$ and ${}_EP$, set against the related $(\theta_1 + \theta_2)$ given by our experiments. Corresponding quantities derived from Stuart and Volkmann's observations (S. and V.) on gases (*Ann. Physik*, 1933, **18**, 121) are inserted throughout.

TABLE 2.

Molecule	$2\delta_0^2 \times 10^3$	$10^{46}A$ from δ_0^2 and ${}_EP$	$10^{46}A$ from S. and V.	$10^{46}A$ from ${}_\infty({}_mK_2)$ and ${}_EP$
CH_3Cl	28·4 [a]	0·050	0·033	0·019 [c]
$CHCl_3$	31·5 [b]	0·191	0·109	0·241 [d]
C_6H_6	77·3 [a]	0·677	0·710	0·290 [c]
	78·2 [b]	0·685		
		$10^{35}\theta_1$ from δ_0^2 and ${}_EP$	$10^{35}\theta_1$ from S. and V.	$10^{35}(\theta_1 + \theta_2)$ from expt.
C_6H_5Me	74·7 [a]	5·42 at 25°	6·32 at 25°	3·02 [c] at 25°
	87·4 [b]	6·34 ,,		
1 : 3-$C_6H_4Me_2$	89·4 [b]	8·51 at 20°	8·39 at 20°	3·09 [c] at 20°

[a] Ref. 2 below Table 4. [b] Ref. 16 below Table 4. [c] From present measurements. [d] ${}_\infty({}_mK_2) = -28{\cdot}5 \times 10^{-12}$ (cf. *J.*, 1953, 4041).

We note a general lack of concordance between the values of A from δ_0^2 and those from ${}_\infty({}_mK_2)$. Where the work of Stuart and Volkmann is concerned, disagreement is restricted to methyl chloride and chloroform; A for benzene, toluene, and *m*-xylene is of the order to be expected from δ_0^2, and—where two estimates of δ_0^2 exist in the literature—from that (higher) δ_0^2 quoted by Cabannes (*op. cit.*).

We have previously (*J.*, 1953, 4041) commented on the fact that, after conversion to

20°, Stuart and Volkmann's K_1 for benzene leads to a molar Kerr constant of *ca.* 17×10^{-12}, whereas for the pure liquid or at infinite dilution in carbon tetrachloride the ${}_mK$ is *ca.* 7×10^{-12}. A similar situation is now revealed for toluene and *m*-xylene, the $\infty({}_mK_2)$ figure for each of which could only be reconciled with its $\delta_0{}^2$ if θ_2 were negative—a condition which is *a priori* unlikely. We are certain of our measured $\infty({}_mK_2)$ values: the system C_6H_6–CCl_4 has been re-examined *de novo* for 8 concentrations, and C_6H_5Me–CCl_4 is here reported for **13**. Either, therefore, θ_1 is unexpectedly solvent-dependent, or Stuart and Volkmann's observations are erroneously large. As to the former possibility, it is relevant that the molar Kerr constants of pure liquid benzene, toluene, or xylene are close to the $\infty({}_mK_2)$ values now found in carbon tetrachloride—no *marked* solvent action is apparent. As to the latter possibility, we have considered the experimental details published by the German authors (*Z. physikal. Chem.*, 1932, **17**, *B*, 429) when recording *B* for benzene vapour as $1{\cdot}8 \times 10^{-10}$. We calculate that, in the apparatus described by them, this corresponds to a phase difference between 0·00005 and 0·00015λ; the threshold of detectability, however, for such optical determinations must be taken to be that (*viz.*, 5×10^{-5} λ) stated by Szivessy (*Z. Physik*, 1921, **6**, 311), who devised the technique used. It is our intention later to reinvestigate benzene and other gases; in the meantime, since our (repeatedly confirmed) measurements involve phase differences of 0·00025—0·02 λ, we feel justified in suspecting both the observations of Stuart and Volkmann *and* the depolarisation factors tabulated by Cabannes, at least when they relate to molecules of low—or no—polarity. Accordingly, procedures whereby b_1, b_2, and b_3 may be deduced without the use of equation (3) become highly desirable, and will be discussed next.

A priori *estimation of* b_3. Table 4 contains data for six derivatives of benzene for which $b_1 = b_2$. (For clarity we mention here our nomenclature for the mutually perpendicular half-axes of the molecular optical polarisability ellipsoids quoted: for a polar molecule, b_1 applies along the direction of action of the resultant dipole moment, and the lesser of the remaining two *b*'s is written as b_3; for a non-polar molecule, the largest polarisability is denoted by b_1 and the smallest by b_3.) In particular, the cases of the tri- and hexa-methyl- and -chloro-benzenes are valuable in providing some support for the assumption that b_3 can be treated additively. In Table 3 we show the differences, Δb_3, between the b_3's observed for a given molecule and the b_3 found for benzene.

TABLE 3. *Values of* $\Delta b_3 \times 10^{23}$ *per molecule and per substituent.*

Molecule	Δb_3 per molecule	Δb_3 per substituent
1 : 3 : 5-$C_6H_3Me_3$	+0·514	+0·171
C_6Me_6	+0·948	+0·158
1 : 3 : 5-$C_6H_3Cl_3$	+0·255	+0·085
C_6Cl_6	+0·455	+0·076
1 : 3 : 5-$C_6H_3Br_3$	+0·669	+0·223
1 : 3 : 5-$C_6H_3(NO_2)_3$	−0·214	−0·071

It is seen that the changes in b_3 caused by three further substituents are somewhat less than those caused by the first three. Such an effect is to be expected on elementary electrostatic theory; it might, however, be connected with non-planarity of the hexa-substituted molecules—a condition which has been suggested for hexachlorobenzene (Bastiansen and Hassel, *Acta Chem. Scand.*, 1947, **1**, 489) and for octamethylnaphthalene but not for hexamethylbenzene (cf. Donaldson and Robertson, *J.*, 1953, 17). By addition to the "found" Δb_3's for benzene of the appropriate "Δb_3 per substituent" (obtained from the 1 : 3 : 5-trisubstituted derivatives) estimates of b_3 for toluene, chlorobenzene, bromobenzene, and nitrobenzene can be produced, and with their help the calculation of b_1 and b_2 for each of these molecules becomes possible. Results are shown in Table 4; they may be compared with the following, deduced from the same $\infty({}_mK_2)$ figures in conjunction with the depolarisation factors also quoted in Table 4.

	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
C_6H_5Me	(Solution unreasonable, see above)		
C_6H_5Cl	1·44$_5$	1·40	0·685
C_6H_5Br	1·66	1·47	0·736
$C_6H_5{\cdot}NO_2$	1·60	1·36	0·690
1 : 3-$C_6H_4Me_2$	(Solution unreasonable, see above)		

It is seen that the values of b_1 obtained for chloro- or bromo-benzene by either method are similar, whereas for nitrobenzene they are substantially identical. For the last named—as for many molecules of high polarity—this is not surprising because ${}_\infty({}_mK_2)^{C_6H_5\cdot NO_2}$ is large, so that $\theta_2^{C_6H_5\cdot NO_2}$ greatly exceeds $\theta_1^{C_6H_5\cdot NO_2}$. Indeed, if θ_1 is neglected and θ_2 solved for the two unknowns b_1 and $(b_2 + b_3)$, these emerge as $1{\cdot}61 \times 10^{-23}$ and $2{\cdot}04 \times 10^{-23}$, respectively; obviously, incorrectness of δ_0^2 is relatively less significant here than it is when θ_1 and θ_2 are not so unequal, or at the extreme—as with toluene or *m*-xylene—of the same order of magnitude. Since in our judgment molar Kerr constants of solutes can be measured with more certainty than depolarisation factors of vapours, we prefer, for these five substances, the entries in Table 4 to the polarisabilities shown a few lines above.

The analyses of the ${}_\infty({}_mK_2)$'s for fluoro-, iodo-, and cyano-benzene remain to be discussed. No depolarisation factors for these compounds are on record, and the method described above cannot be used because the 1 : 3 : 5-trisubstituted benzenes required are either unknown or too insoluble. We therefore propose, *faute de mieux*, to compute b_3 with the help of measurments on the axially symmetric aliphatic analogues.

If we represent the polarisability of a link between two atoms as an ellipsoid having semi-axes, b_L, b_T, and b_V, where subscript L marks the longitudinal polarisability, and T and V mark the two transverse polarisabilities, then for single bonds $b_V = b_T$. Differences shown in Table 3—provided the polarisability of the basic benzenoid skeleton is unaffected by replacement of hydrogen—are clearly estimates of $b_T^{C_{Ar}-X} - b_T^{C_{Ar}-H}$; for the present we shall assume that this quantity is close to $b_3^{CH_3-X} - b_3^{CH_4}$.

Watson and Ramaswamy (*Proc. Roy. Soc.*, 1936, *A*, **156**, 144) have made careful measurements of, *inter alia*, the dispersion of the refractive index of methane, whence ${}_EP^{CH_4} = 6{\cdot}45$ c.c. and by symmetry $b_1^{CH_4} = b_2^{CH_4} = 0{\cdot}254 \times 10^{-23}$. The values of $\Delta b_3 = b_3^{molecule} - b_3^{CH_4}$ are, from Table 4, as follows:

Molecule	CH_3F	CH_3I	$CH_3\cdot CN$
$10^{23} \times \Delta b_3$	−0·022	0·403	0·116

The sums of these with $b_3^{C_6H_6}$ have been taken as the b_3's of the monosubstituted benzenes concerned. Figures so obtained are indicated in Table 4, and in the text below, by braces.

As a check we may apply a parallel procedure to C_6H_5Cl and C_6H_5Br, and compare the b_1 and b_2 so found with those derived from 1 : 3 : 5-trichloro- or -tribromo-benzenes:

	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$		$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
C_6H_5Cl	1·48	1·16	{0·890}	C_6H_5Br	1·69	1·18$_5$	{0·978}
,, ...	1·47	1·24	(0·818)	,, ...	1·68	1·21	(0·956)

It is seen that variations in b_2 affect b_2 rather than b_1, and that b_1 and b_2 by either method are the same to two significant figures.

Table 4 summarises calculations, made in each case by one of the above three methods, for the 29 molecules considered in this paper. Comment on these results can be made more appropriately after the discussion in the next section.

(b) *Calculation of Bond Polarisability Ellipsoids.*—The suggestion referred to above that individual bonds may be described by polarisability ellipsoids was first advanced qualitatively by Meyer and Otterbein (*Physikal. Z.*, 1931, **32**, 290; 1934, **35**, 249). Sachsse (*ibid.*, 1935, **36**, 357), Wang (*J. Chem. Physics*, 1939, **7**, 1012), and Denbigh (*Trans. Faraday Soc.*, 1940, **36**, 936) later attempted to evaluate the half-axes of such ellipsoids from Kerr constant and refractivity data.

In order to simplify the following discussion we shall write $b_L^{C-H} = A$; $b_V^{C-H} = b_T^{C-H} = B$; $b_L^{C-Cl} = C$; $b_V^{C-Cl} = b_T^{C-Cl} = D$; $b_L^{C-C} = E$; and $b_V^{C-C} = b_T^{C-C} = F$.

Both Wang and Denbigh, in evaluating A, B, E, and F, started by adopting tetrahedral angles and using the following expressions:

$$4A/3 + 8B/3 = b_1^{CH_4} \text{ (}ex\text{ molar refraction)} \quad . \quad . \quad . \quad . \quad (5)$$

$$E + 2F + 6A + 12B = (b_1 + b_2)^{C_2H_6} \text{ (}ex\text{ molar refraction)} \quad . \quad . \quad (6)$$

$$E + 2A/3 + 16B/3 = b_1^{C_2H_6} \text{ (}ex\text{ Kerr effect)} \quad . \quad . \quad . \quad . \quad (7)$$

The only other possible equation for a system having A, B, E, and F alone, would have been the following:

$$F + 8A/3 + 10B/3 = b_2^{C_2H_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

thus yielding at first sight four equations and four unknowns; yet on inspection, it is seen that (6) = (7) + twice (8); accordingly there remain three equations and four unknowns. Denbigh did not explicitly quote a fourth equation, but said "similar equations can be set up for other molecules, and, by elimination . . . the longitudinal and transverse polarisabilities of the bonds can be obtained."

TABLE 4. *Calculation of molecular polarisability ellipsoids.*

Solute	Temp.	$10^{35} \times (\theta_1 + \theta_2)$	${}_DP$ (c.c.)	${}_EP$ (c.c.)	$2\delta_0^2 \times 10^3$	μ, D	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$ *
CH_3F	20°	6·73	9 [1]	6·6 [1]	—	1·71	0·316	0·232	0·232
CH_3Cl	25	7·68	13·6 [2]	$11·2_6$ [4]	28·4 [2]	1·72	0·509	0·411	0·411
CH_3Br	25	12·27	14·7 [5]	14·0 [4]	—	1·70	0·656	0·499	0·499
CH_3I	25	12·90	21·9 [6]	18·5 [6]	—	1·48	0·872	0·657	0·657
$CH_3{\cdot}NO_2$	25	21·2	18·3 [7]	12·0 [8]	—	3·14	0·518	0·717	0·183 †
$CH_3{\cdot}CN$	25	52·2	11·7 [9]	$10·8_5$ [10]	—	$3·37_5$	0·543	0·370	0·370
$(CH_3)_3CCl$	25	$20·3_6$	29·3 [6]	24·9 [6]	—	2·14	$1·09_2$	0·926	0·926
$(CH_3)_3CBr$	25	34·7	33·3 [6]	28·3 [6]	—	2·19	$1·29_4$	$1·02_6$	$1·02_6$
$(CH_3)_3CI$	25	48·3	36·9 [6]	33·5 [6]	—	2·14	$1·57_8$	$1·19_1$	$1·19_1$
C_2Cl_6	25	1·09	45·1 [11]	39·6 [12]	—	0	$1·65_7$	$1·65_7$	$1·36_1$
C_6H_6	20	1·72	$26·9_5$ [11]	$25·0_5$ [13]	77·3 [2]	0	$1·11_4$	$1·11_4$	$0·73_3$
C_6H_5Me	25	3·04	32·7 [9]	29·9 [14]	74·7 [2]	0·34	$1·37_7$	$1·25_3$	(0·904)
C_6H_5F	20	13·5	31·3 [6]	24·9 [6]	—	1·38	$1·12_6$	$1·10_6$	{0·711}
C_6H_5Cl	20	34·5	34·9 [15]	29·9 [13]	87·8 [16]	1·59	$1·47_2$	$1·24_4$	(0·818)
C_6H_5Br	25	40·7	35·6 [17]	32·6 [18]	93·8 [16]	1·51	$1·68_4$	$1·21_3$	(0·956)
C_6H_5I	20	44·2	41·4 [6]	38·3 [6]	—	1·39	$1·98_4$	$1·40_7$	{1·136}
$C_6H_5{\cdot}NO_2$	20	255·2	36·2 [15]	30·9 [13]	100 [16]	3·95	$1·60_4$	$1·38_6$	(0·662)
$C_6H_5{\cdot}CN$	20	272·8	33·1 [9]	30·2 [13]	—	4·02	$1·63_8$	$1·21_1$	{0·849}
1 : 2-$C_6H_4Me_2$	20	5·98	35·9 [6]	34·4 [13]	—	0·53	$1·63_9$	$1·35_2$	$(1·07_5)$
1 : 3-$C_6H_4Me_2$	20	3·09	35·9 [6]	34·5 [13]	89·4 [16]	0·26	$1·32_7$	$1·68_2$	$(1·07_5)$
1 : 4-$C_6H_4Me_2$	25	2·52	36·6 [11]	34·6 [13]	—	0	$1·61_3$	$1·40_2$	$(1·07_5)$
1 : 4-$C_6H_4Cl_2$	25	9·18	36·9 [11]	34·7 [13]	—	0	$1·92_3$	$1·27_4$	(0·903)
1 : 4-$C_6H_4Br_2$	20	9·58	40·7 [11]	40·1 [4]	—	0	$2·18_8$	$1·37_3$	$(1·17_9)$
1 : 3 : 5-$C_6H_3Me_3$	20	2·40	41·9 [11]	39·2 [13]	—	0	$1·69_6$	$1·69_6$	$1·24_7$
1 : 3 : 5-$C_6H_3Cl_3$	20	8·94	45·0 [11]	$39·3_5$ [4]	—	0	$1·83_2$	$1·83_2$	0·988
1 : 3 : 5-$C_6H_3Br_3$	20	5·78	50·1 [11]	$47·5_5$ [4]	—	0	$2·10_9$	$2·10_9$	$1·40_2$
1 : 3 : 5-$C_6H_3(NO_2)_3$	25	39·9	54·2 [11]	41·7 [4]	—	0	$2·20_5$	$2·20_5$	$0·51_9$
C_6Me_6	25	3·80	54·6 [11]	52·5 [4]	—	0	$2·26_3$	$2·26_3$	$1·68_1$
C_6Cl_6	20	24·6	63·5 [11]	53·4 [4]	—	0	$2·56_2$	$2·56_2$	$1·18_8$

References. [1] Smyth and McAlpine, *J. Chem. Physics*, 1934, **2**, 499. [2] Cabannes and Granier, *Compt. rend.*, 1926, **182**, 885. [3] Barclay and Le Fèvre, *J.*, 1950, 556. [4] Calc. from atomic refractivities listed by Vogel, *J.*, 1948, 1833. [5] Buckingham and Le Fèvre, *J.*, 1953, 3432. [6] Audsley and Goss, *J.*, 1941, 864; 1942, 358, 497. [7] Smyth and McAlpine, *J. Amer. Chem. Soc.*, 1934, **56**, 1697. [8] Extrapolated from molecular refractions by Vogel, *J.*, 1948, 1852. [9] Taken as $1·05R_D$. [10] Extrapolated from Jeffery and Vogel, *J.*, 1948, 674. [11] *I.e.*, ${}_\infty P_2$. [12] From $R_{C_2HCl_3}$ listed in Landolt–Börnstein's "Tabellen," 1912 Edn., plus constants given in ref. 4. [13] Calc. from molecular refractions listed in ref. 12. [14] Calc. from Vogel, *J.*, 1948, 607. [15] Sugden and Groves, *J.*, 1934, 1094. [16] Cabannes, *op. cit.*, Chap. XIII. [17] Groves and Sugden, *J.*, 1935, 971. [18] Extrapolated from Vogel, *J.*, 1948, 657.

* Values in parentheses in this column are calculated from $b_3^{C_2H_4}$ and data in Table 3; those in braces are explained in the text. Except for nitromethane, all others are derived by direct computation from ${}_\infty(_mK_2)$ and other observations now recorded.

† $b_3^{CH_3\cdot NO_2}$ calc. as $b_3^{CH_4} - 0·07$ (from Table 3). If the assumption be made for nitromethane that $b_2 = b_3$, then $b_1 = 0·527$, and $b_2 = b_3 = 0·446 \times 10^{-23}$.

Wang introduced b_1; b_2, and b_3 for acetone, and thus provided three new relations containing—as he supposed—two further unknowns only, *viz.*, $b_L^{C=O}$ and $b_T^{C=O}$; however, Wang's underlying assumption, that $b_T^{C=O} = b_V^{C=O}$, is one with which we cannot agree. In general, attempts to solve for A, B, etc., by adding to an A, B, E, F system a double linkage (which would give rise to three extra and different expressions for b_1, b_2, and b_3 of the derivative) must fail. Inevitably with the three new equations there will be produced as many new unknowns. If, instead, we add C–R or C≡R, where $b_L^{C-R} \neq b_T^{C-R} = b_V^{C-R}$ or $b_L^{C\equiv R} \neq b_T^{C\equiv R} = b_V^{C\equiv R}$, then admittedly we add only two unknowns, but the molecule under consideration will have an axis of symmetry and accordingly one equation is lost.

In conclusion, we submit that, if the tetrahedral arrangement of methane and its derivatives is to be assumed, it is not possible to evaluate A, B, C, and D by the additivity methods discussed so far. We instance the following example to substantiate our point:

$$A + 2B = 0{\cdot}75\alpha^{CH_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$C + 2D = 0{\cdot}75\alpha^{CCl_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$A/3 + 8B/3 + C = b_1^{CH_3Cl} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$4A/3 + 5B/3 + D = b_2^{CH_3Cl} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$C/3 + 8D/3 + A = b_1^{CHCl_3} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$4C/3 + 5D/3 + B = b_2^{CHCl_3} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

One might reasonably expect solution of A, B, C, and D from the above expressions (9)—(14), but $\alpha^{CH_4} + \alpha^{CCl_4} = \alpha^{CH_3Cl} + \alpha^{CHCl_3}$, *i.e.*,

$$4/3(9) + 4/3(10) = 1/3\{(11) + 2(12)\} + 1/3\{(13) + 2(14)\}$$

or, (11), (12), (13), (14) are together transformable into (9) and (10), and accordingly we are reduced to two equations only, *viz.*, (9) and (10), with the four unknowns A, B, C, and D. The same argument applies to any attempted handling on similar lines of A, B, C, and D from polarisability data drawn from all (tetrahedral) structures containing the links to which A, B, etc., relate.

Sachsse differed from Denbigh and Wang in taking account, where possible, of deviations from regular tetrahedral configurations; *via* appropriate equations for, *e.g.*, CH_3Cl, CH_2Cl_2, and $CHCl_3$, he obtained numerical values for A, B, C, D, etc. In particular, he found A and B to be $0{\cdot}081 \times 10^{-23}$ and $0{\cdot}057 \times 10^{-23}$, respectively. These figures are not dissimilar from those of Wang ($0{\cdot}072 \times 10^{-23}$ and $0{\cdot}062 \times 10^{-23}$) or Denbigh ($0{\cdot}079 \times 10^{-23}$ and $0{\cdot}058 \times 10^{-23}$), despite the criticisms indicated above. This, we suggest, is because A and B are both small and nearly equal; indeed if, following Ingold ("Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953), we take $A = B$, then from (9) and ${}_gP^{CH_4}$ (Watson and Ramaswamy, *loc. cit.*), $A = B = 0{\cdot}064 \times 10^{-23}$. Since the slight inconsistencies in A and B scarely affect the main objective of this paper, and because Sachsse's derivation seems the most firmly based, we propose to accept his values, rounding them off to $A = 0{\cdot}08 \times 10^{-23}$ and $B = 0{\cdot}06 \times 10^{-23}$.

From the $b_1^{CH_4}$ previously quoted (Watson and Ramaswamy, *loc. cit.*) the polarisabilities of the methyl radical follow as $b_1^{CH_3} = 0{\cdot}17 \times 10^{-23}$ and $b_2^{CH_3} = b_3^{CH_3} = 0{\cdot}19 \times 10^{-23}$. At once, by appropriate subtractions from the b's of Table 4, estimates can be made of b_L^{C-X}, b_T^{C-X}, and b_V^{C-X}. (The directions indicated by the subscripts L, V, and T are related to b_1, b_2, and b_3 respectively in a molecule R–X.) Examples are included in Table 5. The C–C bond ellipsoid can be similarly deduced from ethane: Breazeale (*loc. cit.*) gives $B^{C_2H_6}$ as $10{\cdot}4 \times 10^{-12}$ at N.T.P.; $({}_mK_{gas})^{N.T.P.}$ is therefore $1{\cdot}122 \times 10^{-12}$, and—since ${}_DP = 11{\cdot}16$ c.c. (Watson and Ramaswamy, *loc. cit.*)—$b_1^{C_2H_6} = 0{\cdot}536 \times 10^{-23}$ and $b_2^{C_2H_6} = b_3^{C_2H_6} = 0{\cdot}386 \times 10^{-23}$; after allowance for two methyl groups, b_L^{C-C} is seen to be $0{\cdot}20 \times 10^{-23}$ and b_T^{C-C} to be $0{\cdot}01 \times 10^{-23}$.

Polarisabilities of Molecules related as Alphyl–X and Aryl–X.—The comparison may be made by the procedure explained by Ingold (*op. cit.*): from the molecular b's listed in Table 4 we subtract the appropriate b_1, b_2, or b_3 of the radicals methyl or phenyl. (The former have been already given; the latter, from the results for C_6H_6 and the C–H bond, are: $b_1 = 1{\cdot}03 \times 10^{-23}$, $b_2 = 1{\cdot}05 \times 10^{-23}$, and $b_3 = 0{\cdot}67 \times 10^{-23}$). The upper part of Table 5 is thus obtained; the lower part shows the differences between the corresponding b_L's, b_V's, etc., for aryl–X and alphyl–X links in the phenyl and methyl compounds.

We note at once that, except with the C–CH_3 link, the algebraic sign of the largest Δb in each case is the same as that of the exaltation of refraction revealed by a parallel treatment of refractivity data and listed by Ingold (*op. cit.*, p. 127). The Δb_i's of Table 4 thus seem, in part, harmonious with a conclusion already reached by this author, namely that the ". . . exaltation of polarisability produced by substituents . . . in aromatic combination, is concentrated along the dipole axis: indeed this exaltation is augmented

at the expense of polarisability in other directions. The whole effect is not very great for CH_3, but is larger for Cl . . . " (*op. cit.*, pp. 136, 137).

TABLE 5.* *Principal axes for* C–X *in various methyl and phenyl compounds.*

Compound	b_L	b_V	b_T	Compound	b_L	b_V	b_T
CH_3F	0·15	0·04	0·04	C_6H_5F	0·10	0·06	0·04
CH_3Cl	0·34	0·22	0·22	C_6H_5Cl	0·44	0·19	0·15
CH_3Br	0·49	0·31	0·31	C_6H_5Br	0·65	0·16	0·29
CH_3I	0·70	0·47	0·47	C_6H_5I	0·95	0·36	0·47
$CH_3{\cdot}CN$	0·37	0·18	0·18	$C_6H_5{\cdot}CN$	0·61	0·16	0·18
$CH_3{\cdot}NO_2$	0·35	0·53	−0·01	$C_6H_5{\cdot}NO_2$	0·57	0·34	−0·01
$CH_3{\cdot}CH_3$	0·37	0·20	0·20	C_6H_5Me	0·35	0·20	0·23

$$\Delta b_i = b_i^{\text{Aryl-X}} - b_i^{\text{Alphyl-X}}$$

	Δb_L	Δb_V	Δb_T		Δb_L	Δb_V	Δb_T
C–F	−0·05	+0·02	0	C–CN	+0·24	−0·02	0
C–Cl	+0·10	−0·03	−0·07	$C–NO_2$	+0·22	−0·19	0
C–Br	+0·16	−0·15	−0·03	$C–CH_3$	−0·02	0	+0·03
C–I	+0·25	−0·11	0				

* Units = 10^{-23} c.c.

Similar directed exaltations may be inferred for the disubstituted benzenes, both polar and non-polar, included in Table 4. When the bond values in Table 5, together with those for C–H and C–C already noted, are used in conjunction with b_1, b_2, and b_3 of benzene, the ellipsoid of a given structure $C_6H_4X_2$ can be computed and compared with that deduced from experiment; Table 6 summarises such calculations.

TABLE 6.* *Directed exaltations in molecules of type* $C_6H_4X_2$.

	Calculated			Found			Exaltations		
	b_1	b_2	b_3	b_1	b_2	b_3	Δb_1	Δb_2	Δb_3
1 : 2-$C_6H_4Me_2$	$1{\cdot}61_5$	$1{\cdot}46_5$	1·01	1·64	1·35	$1{\cdot}07_5$	$+0{\cdot}02_5$	$-0{\cdot}11_5$	$+0{\cdot}06_5$
1 : 3-$C_6H_4Me_2$	$1{\cdot}46_5$	$1{\cdot}61_5$	1·01	1·32	1·68	$1{\cdot}07_5$	$-0{\cdot}14_5$	$+0{\cdot}06_5$	$+0{\cdot}06_5$
1 : 4-$C_6H_4Me_2$	1·69	1·39	1·01	1·61	1·40	$1{\cdot}07_5$	−0·08	+0·01	$+0{\cdot}06_5$
1 : 4-$C_6H_4Cl_2$	1·63	1·43	1·05	1·92	1·28	0·90	+0·29	−0·15	−0·15
1 : 4-$C_6H_4Br_2$	1·93	1·61	1·23	2·19	1·37	1·18	+0·26	−0·24	−0·05

* Units = 10^{-23} c.c.

With the two dihalogenobenzenes the positive exaltations along the 1 : 4-axes are notable, and compatible with the quoted statement by Ingold. Our results for the xylenes, however, resemble those for toluene in showing effects which, although slight, do not seem reconcilable either with the small positive exaltations of molecular refraction recognisable in these molecules or with the idea that such exaltations occur mainly along the CH_3–C bond directions. Unavoidable errors could produce this situation: for example, if the longitudinal polarisability of the CH_3–C_{Alphyl} link were lower than that shown in Table 5 by only 0·02—0·04 unit, the difficulty would vanish; the figure in question is derived from the sole available measurements of the Kerr constant of ethane, those by Breazeale, on the gas, using light of λ 6500 Å; and $b_1^{C_1H_4}$ derived therefrom may be a little too high. Incidentally, the last point directly affects the magnitudes of b_L^{C-C} and b_T^{C-C}: taking these as $0{\cdot}20 \times 10^{-23}$ and $0{\cdot}01 \times 10^{-23}$ leads to a calculated average refractivity for the C–C bond of 1·8—1·9 c.c., whereas from a recent analysis (Vogel, Cresswell, Jeffery, and Leicester, *J.*, 1952, 514) *ca.* 1·3 c.c. seems most probable. A similar check on the other bond data of this paper is made in Table 7.

TABLE 7. *Calculated and found bond refractions.*

Bond	Mean R_{Bond} calc. ex Table 5 (c.c.)		Mean R_{Bond} given by Vogel *et al.* for *D* line (c.c.)	
	Aliphatic	Aromatic	Aliphatic	Aromatic
C–F	1·9	1·7	1·4 *	1·5
C–Cl	6·6	6·6	6·5	6·6
C–Br	9·4	9·3	9·4	9·5
C–I	13·9	15·1	14·6	14·6
$C–NO_2$	7·4	7·6	7·4	8·2
C–CN	6·2	8·0	6·1	7·1
$C–CH_3$	6·5	6·5	6·3	6·6

* Vogel *et al.* annotate their figures for C–F as " preliminary values."

It appears that our figures for b_L^{C-F} and b_T^{C-F} are probably high (the observations on methyl fluoride–carbon tetrachloride mixtures were the most troublesome to make, and therefore the least certain experimentally, of all in this paper); however, Vogel *et al.* call their results for the fluoro-group " preliminary," and we note that their Tables 51 and 53 indicate for fluorobenzene an exaltation of about 0·04 c.c., which is positive, not negative as concluded from other sources by Ingold (*op. cit.*, p. 127) and as shown in our Table 5 under Δb_L. The remaining cases in Table 7 display consistency which is reasonable in view of the larger b_L, b_T, and b_V data involved. Regarding b_L^{C-H} and b_T^{C-H}, the values adopted in this work lead to $R_{C-H} = 1{\cdot}7$ c.c., in satisfactory accord with that reported by Vogel *et al.* for this bond.

The above questions directly concern the degree to which bond polarisability ellipsoids are constant throughout a range of different molecular structures involving them; it is relevant therefore now to consider the *tert.*-butyl halides (included in Table 4) in the same way as we already have the phenyl halides.

From the refractivity of *neo*pentane we estimate R_∞ to be 25·0 c.c., whence $b_1 = b_2 = b_3 = 0{\cdot}986 \times 10^{-23}$ c.c. After subtracting the polarisabilities appropriate for three C–H links and one C–C link (and assuming retention of tetrahedral angles), we obtain for the $(CH_3)_3C$ unit : $b_1 = 0{\cdot}62 \times 10^{-23}$ and $b_2 = b_3 = 0{\cdot}79 \times 10^{-23}$ c.c. Table 8 lists the principal axes which then follow for the carbon–halogen links in the three molecules

TABLE 8. tert.-*Butyl halides.**

Link	b_L	$b_V = b_T$	Δb_L †	$\Delta b_V = \Delta b_T$ †
C–Cl	0·47	0·14	+0·13	−0·06
C–Br	0·67	0·24	+0·18	−0·07
C–I	0·96	0·40	+0·26	−0·07

* Units : 10^{-23} c.c. † $\Delta b_i = (b_i^{C-X})_{tert.\text{-butyl halide}}$ minus $(b_i^{C-X})_{\text{methyl halide}}$.

$(CH_3)_3CX$, together with their differences from the corresponding values for the related CH_3–X structures. Positive exaltations along the axes of the bonds, and negative exaltations across them, thus seem to occur.

Finally, we refer to the case of hexachloroethane. The molar Kerr constant of this substance was determined by Sachsse (*loc. cit.*) who reported it as $4{\cdot}9 \times 10^{-12}$. Our work confirms the low order of this value, and provides estimates of polarisability of $1{\cdot}36 \times 10^{-23}$ c.c. along the C–C direction and of $1{\cdot}66 \times 10^{-23}$ for the two perpendicular directions. In theory, information on the C–C link should now be accessible either *via* data on chloroform ($b_1 = 0{\cdot}59 \times 10^{-23}$, $b_2 = b_3 = 0{\cdot}93_5 \times 10^{-23}$; Le Fèvre and Le Fèvre, *loc. cit.*) and the C–H bond (this paper), or data on carbon tetrachloride ($b_1 = b_2 = b_3 = 1{\cdot}013 \times 10^{-23}$) and the C–Cl bond (this paper). However, the former method produces a negative quantity for b_T^{C-C}. This is probably because the spatial arrangement of the CCl_3 group in chloroform is not retained in hexachloroethane; elementary reasoning from volume requirements would suggest that the Cl–C–Cl angles in C_2Cl_6 should be less than those in $CHCl_3$. The latter route, starting from CCl_4 and C–Cl link data from Table 5, yields $b_L^{C-C} = 0{\cdot}02 \times 10^{-23}$ c.c. and $b_T^{C-C} = 0{\cdot}08 \times 10^{-23}$ c.c.

These values are in marked contrast to those drawn from methane and ethane, although they resemble Sachsse's results, which are $b_L^{C-C} = 0{\cdot}02 \times 10^{-23}$ and $b_T^{C-C} = 0{\cdot}05 \times 10^{-23}$ c.c. It is possible that the electron attracting $(-I)$ actions of the six chlorine atoms exert a "polarity" effect on the C–C bond, making its electrons more tightly bound than those between the carbon atoms of ethane, so that a smaller C–C polarisability in C_2Cl_6 than in C_2H_6 merely parallels the general diminishing order known for the polarisabilities of negatively charged, neutral, and positively charged atoms; alternatively, although it seems unlikely, hexachloroethane may be subject to double halogen hyperconjugation. Whatever the explanation, the case is a warning against accepting the anisotropic polarisabilities of bonds as constants throughout all molecular situations.

Conclusions.—Our measurements indicate (1) that changes in average polarisability consequent upon the introduction of a substituent with $\pm M$ character into the benzene ring are not uniformly distributed but tend to be " oriented in the direction along which the hyperconjugative or conjugative electromeric polarisability, allowed by the substituent,

should be effective" (Ingold, *op. cit.*, p. 137), and (2) that in the *tert.*-butyl halides each C–Halogen bond shows an enhanced longitudinal polarisability, the increases running I > Br > Cl; such effects may be a manifestation of inductomeric polarisability, for which this order of the halogens, and the greater effect with $(CH_3)_3C$ than with CH_3, is to be expected (cf. Ingold, *op. cit.*, p. 73).

Experimental

Materials.—Carbon tetrachloride and benzene for use as solvents were both sulphur-free. We thank Messrs. I.C.I. (Australia and New Zealand) Ltd. for the gift of a bulk supply of the former, selected specially from a "middle cut." After drying ($CaCl_2$), fractionation, and storage over calcium chloride, it showed B values similar to those of most carefully purified specimens of "AnalaR" grade, and was therefore given no further treatment. Thiophen-free benzene was partially frozen, and the remelted solid kept over clean sodium wire.

The solutes were redistilled or recrystallised, as appropriate, before use and had the b. p.s or m. p.s recorded for pure samples in Beilstein's "Handbuch." The methyl bromide was part of that used for other work (cf. Buckingham and Le Fèvre, *J.*, 1953, **3432**). Methyl fluoride was generated as required by heating together potassium fluoride and potassium methyl sulphate (Batuecas and Moles, *J. Chim. phys.*, 1919, **17**, 537). Methyl chloride was obtained from methyl alcohol (Barclay and Le Fèvre, *J.*, 1950, 556). Gases were dissolved by a technique similar to that used by Le Fèvre and Ross (*J.*, 1950, 283) for sulphur dioxide.

Measurements.—These were made by the methods described in our previous paper (*J.*, 1953, 4041), where the symbols used here are defined, and the extrapolation procedure explained. The observations recorded in Table 9 are for either 20° or 25°, at which temperatures the following data for the solvents are taken:

Temp.	10^7B_D	n_D	d_4^t	ε_t	H	J	$10^{14}{}_sK_1$
			Carbon tetrachloride.				
20°	0·072	1·4604	1·5940	2·2360	2·064	0·4721	0·761
25	0·070	1·4575	1·5845	2·2270	2·060	0·4731	0·749
			Benzene				
20	0·424	1·5010	0·8791	2·2825	2·119	0·4670	7·72
25	0·410	1·4973	0·8738	2·2725	2·114	0·4681	7·56

TABLE 9. *Weight-fractions, Kerr constants, refractive indexes, densities, and dielectric constants of solutions.*

10^5w_2	10^7B_{12}	$(n_D{}^t)_{12}$	$(d_4{}^t)_{12}$	$(\varepsilon_t)_{12}$	10^5w_2	10^7B_{12}	$(n_D{}^t)_{12}$	$(d_4{}^t)_{12}$	$(\varepsilon_t)_{12}$
Methyl fluoride in carbon tetrachloride at 20°.									
15	$0·072_5$	—	1·5937	2·2366	98	0·081	1·4598	1·5922	2·2540
26	$0·074_5$	—	1·5935	2·2398	101	0·082	1·4600	1·5921	2·2535
29	0·075	—	1·5935	2·2395	119	0·083	1·4598	1·5921	2·2539
34	0·075	—	1·5934	2·2417	185	0·085	1·4595	1·5904	2·2660
Whence $\Sigma(\Delta B \,.\, w_2)/\Sigma w_2{}^2 = 8·2_5$.									
Methyl chloride in carbon tetrachloride at 25°.									
180	0·084	1·4573	1·5821	2·2466	922	0·135	1·4557	1·5745	2·3275
390	0·098	1·4569	1·5804	2·2695	971	0·136	1·4556	1·5739	2·3328
882	0·122	1·4558	1·5749	2·3239	1184	0·153	1·4552	1·5717	2·3568
889	0·133	1·4558	1·5747	2·3240	1441	0·174	1·4547	1·5688	2·3846
Whence $\Delta B = 6·21w_2 + 67w_2{}^2$.									
Methyl bromide in carbon tetrachloride at 25°.									
24	0·080	1·4575	1·5846	2·2284	859	0·115	1·4571	1·5852	2·2754
497	0·095	1·4573	1·5849	2·2555	984	0·122	1·4571	1·5853	2·2829
611	0·101	1·4572	1·5850	2·2617	1004	0·121	1·4571	1·5854	2·2833
732	0·108	1·4572	1·5851	2·2685	1866	0·166	1·4568	1·5858	2·3318
Whence $\Delta B = 5·20w_2 - 3·0w_2{}^2$.									
Methyl iodide in carbon tetrachloride at 25°.									
1148	0·117	1·4580	1·5899	2·2626	6705	0·322	1·4605	1·6153	2·4348
2675	0·167	1·4589	1·5968	2·3126	7689	0·350	1·4608	1·6206	2·4730
2938	0·175	1·4590	1·5980	2·3210	9171	0·408	1·4616	1·6258	2·5296
5502	0·270	1·4598	1·6098	2·4031					
Whence $\Delta B = 3·63w_2 - 0·23w_2{}^2$									

TABLE 9. (*Continued.*)

10^5w_2	10^7B_{12}	$(n_D')_{12}$	$(d_4')_{12}$	$(\varepsilon_l)_{12}$	10^5w_2	10^7B_{12}	$(n_D')_{12}$	$(d_4')_{12}$	$(\varepsilon_l)_{12}$
Nitromethane in benzene at 25°.									
1019	0·522	1·4961	0·87590	2·4499	2902	0·759	1·4940	0·87978	2·7774
1287	0·559	1·4958	0·87646	2·4951	3277	0·782	1·4936	0·88060	2·8394
2411	0·676	1·4946	0·87879	2·6944	4016	0·885	1·4927	0·88213	2·9713
Whence $\Delta B = 10{\cdot}90w_2 + 22{\cdot}1w_2^2$.									
Acetonitrile in carbon tetrachloride at 25°.									
366	0·266	1·4565	1·5785	2·4283	1423	0·829	1·4538	1·5610	3·0182
485	0·340	1·4562	1·5765	2·4938	2015	1·095	1·4522	1·5510	3·3352
735	0·515	1·4555	1·5724	2·6386	3369	1·894	1·4486	1·5287	4·1136
1073	0·603	1·4547	1·5668	2·8301					
Whence $\Delta B = 51{\cdot}6_5w_2 + 63w_2^2$.									
tert.-Butyl chloride in carbon tetrachloride at 25°.									
104	0·087	1·4574	1·5831	2·2367	1483	0·200	1·4559	1·5645	2·3659
670	0·134	1·4570	1·5753	2·2897	2067	0·255	1·4552	1·5568	2·4208
1020	0·153	1·4562	1·5705	2·3226	2394	0·279	1·4546	1·5524	2·4516
Whence $\Delta B = 8{\cdot}80w_2 - 0{\cdot}20w_2^2$.									
tert.-Butyl bromide in carbon tetrachloride at 25°.									
570	0·130	—	1·5817	2·2657	1957	0·301	1·4574	1·5747	2·3601
1220	0·210	1·4575	1·5785	2·3111	3643	0·576	1·4573	1·5670	2·4765
1791	0·291	1·4574	1·5756	2·3470					
Whence $\Delta B = 10{\cdot}1w_2 + 103w_2^2$.									
tert.-Butyl iodide in carbon tetrachloride at 25°.									
567	0·123	1·4576	1·5834	2·2503	2651	0·331	1·4583	1·5795	2·3516
1734	0·240	$1{\cdot}4579_5$	1·5807	2·2997	3110	$0{\cdot}379_5$	$1{\cdot}4583_5$	1·5786	2·3731
2048	0·273	1·4580	1·5806	2·3273	3706	0·435	1·4586	1·5776	2·4190
Whence $\Delta B = 10{\cdot}4w_2 - 17w_2^2$.									
Hexachloroethane in carbon tetrachloride at 25°.									
607	0·072	1·4579	1·5855	2·2289	2495	0·078	1·4590	1·5890	2·2334
995	0·073	1·4580	1·5862	2·2295	3045	0·080	—	—	—
1146	0·073	1·4581	1·5865	2·2300	5292	0·099	—	—	—
2476	0·078	1·4589	1·5889	2·2332					
Whence $\Delta B = 0{\cdot}131w_2 + 7{\cdot}7w_2^2$.									
Benzene in carbon tetrachloride at 20°.									
2325	0·081	1·4624	1·5761	2·2412	6,832	0·122	1·4669	1·5098	2·2510
3893	0·097	1·4639	1·5444	2·2447	9,064	0·135	1·4694	1·4835	2·2559
4110	0·100	1·4644	1·5424	2·2468	10,806	0·148	1·4714	1·4655	2·2613
6085	0·109	1·4664	1·5198	2·2500	17,673	0·174	1·4779	1·3785	2·2749
Whence $\Delta B = 0{\cdot}756w_2 - 0{\cdot}96w_2^2$.									
Toluene in carbon tetrachloride at 25°.									
1524	0·092	—	—	—	7205	0·165	1·4625	1·4952	2·2687
1593	0·093	1·4586	1·5849	2·2362	7651	0·168	1·4629	1·4893	2·2717
2883	0·104	1·4594	1·5490	2·2437	8666	0·187	—	—	—
2968	0·106	1·4596	1·5480	2·2440	12,276	0·248	—	—	—
4774	0·133	1·4608	1·5237	2·2548	17,707	0·351	—	—	—
6717	0·160	1·4624	1·5012	2·2658	21,185	0·422	—	—	—
6972	0·176	—	—	—					
Whence $\Delta B = 1{\cdot}19w_2 + 2{\cdot}2w_2^2$.									
Fluorobenzene in carbon tetrachloride at 20°.									
1156	0·139	1·4605	1·5833	2·2880	1729	0·175	1·4605	1·5784	2·3103
1458	0·159	1·4605	1·5806	2·2988	1853	0·180	1·4605	1·5770	2·3156
1602	0·164	1·4605	1·5794	2·3049	3637	0·296	1·4607	1·5619	2·3909
Whence $\Delta B = 5{\cdot}628w_2 + 14{\cdot}5w_2^2$.									
Bromobenzene in carbon tetrachloride at 25°.									
806	0·155	—	1·5837	2·2534	2411	0·324	1·4600	1·5822	2·3015
1122	0·188	1·4587	1·5835	2·2615	2599	0·355	1·4603	1·5820	2·3068
1398	0·213	—	1·5832	2·2698	2664	0·361	1·4604	1·5818	2·3083
1700	0·252	1·4594	1·5827	2·2795	3114	0·408	1·4607	1·5812	2·3220
Whence $\Delta B = 10{\cdot}19w_2 + 23{\cdot}6w_2^2$.									
Iodobenzene in carbon tetrachloride at 20°.									
337	0·108	1·4609	1·5947	2·2441	4881	0·492	1·4675	1·6042	2·3512
662	0·131	1·4613	1·5954	2·2509	5302	0·534	1·4680	1·6051	2·3580
2865	0·320	1·4645	1·6002	2·3019	5649	0·566	1·4685	1·6059	2·3654
Whence $\Delta B = 8{\cdot}642w_2 + 1{\cdot}04w_2^2$.									

TABLE 9. (*Continued.*)

10^5w_2	10^7B_{12}	$(n_D^f)_{12}$	$(d_4^f)_{12}$	$(\varepsilon_i)_{12}$	10^5w_2	10^7B_{12}	$(n_D^f)_{12}$	$(d_4^f)_{12}$	$(\varepsilon_i)_{12}$
Benzonitrile in carbon tetrachloride at 20°.									
86	0·171	1·4605	1·5932	2·2632	404	0·512	1·4609	1·5903	2·3633
317	0·433	1·4608	1·5912	2·3363	788	0·930	1·4613	1·5870	2·4838
400	0·508	1·4609	1·5904	2·3623	926	1·141	1·4615	1·5858	2·5271
Whence $\Delta B = 106{\cdot}2w_2 + 778w_2^2$.									
o-Xylene in carbon tetrachloride at 20°.									
1546	0·104	1·4618	1·5742	2·2457	6501	0·206	1·4665	—	—
2465	0·125	1·4626	1·5622	2·2522	8097	0·236	1·4680	1·4956	2·2866
5870	0·193	1·4660	1·5190	2·2730	8299	0·242	1·4681	—	—
Whence $\Delta B = 2{\cdot}14w_2 - 1{\cdot}3w_2^2$.									
m-Xylene in carbon tetrachloride at 20°.									
996	0·079	1·4609	1·5805	2·2395	9,970	0·176	1·4670	1·4695	2·2610
4542	0·119	1·4633	1·5344	2·2486	16,138	0·233	1·4705	1·4013	2·2783
9839	0·174	1·4668	1·4703	2·2601	18,980	0·266	1·4720	1·3725	2·2891
Whence $\Delta B = 1{\cdot}044w_2 - 0{\cdot}16w_2^2$.									
p-Xylene in carbon tetrachloride at 25°.									
1248	0·079	1·4584	1·5677	2·2302	8,711	0·145	1·4634	1·4752	2·2396
2165	0·086	1·4590	1·5564	2·2313	11,461	0·165	1·4662	1·4554	2·2499
3898	0·093	1·4603	1·5336	2·2340	43,240	0·427	1·4817	—	2·3138
Whence $\Delta B = 0{\cdot}816w_2 + 0{\cdot}14w_2^2$.									
p-Dichlorobenzene in carbon tetrachloride at 25°.									
303	0·076	1·4580	1·5836	2·2279	1754	0·108	1·4600	1·5793	2·2325
754	0·090	1·4585	1·5822	2·2293	1939	0·112	1·4603	1·5786	2·2330
1297	0·098	1·4595	1·5806	2·2310	2171	0·118	1·4605	1·5780	2·2338
Whence $\Delta B = 2{\cdot}38_5w_2 - 10w_2^2$.									
p-Dibromobenzene in carbon tetrachloride at 20°.									
1261	0·093	1·4620	1·5980	2·2391	1746	0·101	1·4626	1·5995	2·2404
1521	0·097	1·4623	1·5990	2·2398	1985	0·105	—	—	—
1731	0·100	—	—	—	2081	0·107	—	—	—
Whence $\Delta B = 1{\cdot}57_5w_2 + 4{\cdot}6w_2^2$.									
Mesitylene in carbon tetrachloride at 20°.									
189	0·073	1·4604	1·5915	2·2363	2507	0·090	1·4618	1·5602	2·2403
285	0·073	1·4604	1·5902	2·2366	3432	0·096	1·4624	1·5477	2·2418
955	0·077	1·4610	1·5810	2·2376	5419	0·110	1·4637	1·5222	2·2445
Whence $\Delta B = 0{\cdot}668w_2 + 0{\cdot}69w_2^2$.									
1 : 3 : 5-Trichlorobenzene in carbon tetrachloride at 20°.									
460	0·080	1·4609	1·5930	2·2378	1529	0·100	1·4622	1·5910	2·2424
1148	0·092	1·4617	1·5918	2·2406	2710	0·117	1·4635	1·5887	2·2468
1339	0·096	1·4620	1·5915	2·2414					
Whence $\Delta B = 1{\cdot}90w_2 - 8{\cdot}7w_2^2$.									
1 : 3 : 5-Tribromobenzene in carbon tetrachloride at 20°.									
424	0·075	1·4609	1·5962	2·2375	1413	0·083	—	—	—
1025	0·079	—	—	—	1451	0·083	1·4622	1·6013	2·2407
1149	0·082	1·4618	1·5998	2·2396	1849	0·087	—	—	—
Whence $\Delta B = 0{\cdot}698w_2 + 6{\cdot}0w_2^2$.									
1 : 3 : 5-Trinitrobenzene in benzene at 25°.									
10^5w_2		542		713	974		1106	2204	2388
10^7B_{12}		0·428		0·438	0·437		0·455	0·469	0·472
$(n_D)_{12}^{25}$		1·4976		1·4978	1·4979		1·4980	1·4985	1·4987
Whence $\Delta B = 4{\cdot}12_5w_2 - 64w_2^2$.									
10^5w_2	10^7B_{12}	$(n_D^f)_{12}$	$(d_4^f)_{12}$	$(\varepsilon_i)_{12}$	10^5w_2	10^7B_{12}	$(n_D^f)_{12}$	$(d_4^f)_{12}$	$(\varepsilon_i)_{12}$
Hexamethylbenzene in carbon tetrachloride at 25°.									
219	0·072	1·4580	1·5821	2·2275	1142	0·081	1·4594	1·5719	2·2299
579	0·075	1·4584	1·5781	2·2276	1732	0·080	1·4608	1·5655	2·2322
691	0·076	1·4585	1·5769	2·2287	2768	0·089	1·4628	1·5540	2·2337
896	0·076	1·4592	1·5746	2·2290					
Whence $\Delta B = 0{\cdot}819w_2 - 5{\cdot}6w_2^2$.									
Hexachlorobenzene in benzene at 20°.									
248	$0{\cdot}428_5$	—	—	—	1351	0·451	1·5020	0·8852	2·2867
878	0·441	1·5016	0·8831	2·2859	1738	0·459	1·5023	0·8870	2·2872
935	0·442	—	—	—	2474	0·547	1·5028	0·8904	2·2905
Whence $\Delta B = 1{\cdot}88w_2 + 7{\cdot}6w_2^2$.									

From the information contained in Table 9, molar Kerr constants at infinite dilution are calculated in Table 10. Since $\alpha\varepsilon_1$, γn_1, and βd_1 do not affect the results very critically they have been estimated in all cases as the quotients: Σ(differences between solutions and solvent)/Σw_2. In deducing the standard errors of $B_1\delta$, the equations quoted by Harris, Le Fèvre, and Sullivan (*J.*, 1953, 1622) have been utilised, the quantities ΔB replacing those written as δQ by these authors.

TABLE 10. *Calculation of molar Kerr constants at infinite dilution.*

Temp.	Solute	Solvent	$\alpha\varepsilon_1$	β	γ	δ	±% Std. error on $B_1\delta$	No. of solns. giving $B_1\delta$	$_\infty(_mK_2) \times 10^{12}$
20°	CH_3F	CCl_4	16	−1·15	−0·34	114	10·5	8	28·3
25	CH_3Cl	,,	10·9	−0·690	−0·130	88·7	6·0	8	32·3
25	CH_3Br	,,	5·72	0·051	−0·028	74·3	1·3	8	51·6
25	CH_3I	,,	3·20	0·290	0·031	51·9	3·8	7	$54·2_5$
25	CH_3NO_2	C_6H_6	17·4	0·238	−0·076	26·6	3·5	6	89·0
25	$CH_3{\cdot}CN$	CCl_4	55·7	−1·044	−0·181	738	2·8	7	219·5
25	$(CH_3)_3CCl$	,,	9·37	−0·852	−0·077	126	3·6	6	85·6
25	$(CH_3)_3CBr$	,,	6·81	−0·309	−0·003	144	2·5	5	146
25	$(CH_3)_3CI$	,,	4·77	−0·121	0·019	149	2·6	6	203
25	C_2Cl_6	,,	0·259	0·111	0·039	1·87	6·0	7	4·60
20	C_6H_6	,,	0·227	−0·755	0·067	10·5	5·1	8	7·24
25	$C_6H_5{\cdot}CH_3$	,,	0·511	−0·784	0·048	17·0	1·9	13	12·8
20	C_6H_5F	,,	4·31	−0·567	0·005	78·2	1·4	6	56·8
20	C_6H_5Cl	,,	4·84	−0·431	0·043	170	1	8	145 *
25	C_6H_5Br	,,	3·10	−0·075	0·073	146	1·6	8	171
20	C_6H_5I	,,	2·31	0·132	0·099	120	0·8	6	186
20	$C_6H_5{\cdot}NO_2$	CCl_4	25·6	−0·322	0·063	1156	1	8	1073 *
20	$C_6H_5{\cdot}CN$	,,	31·5	$-0·560_5$	0·082	1475	2·5	6	1147
20	1 : 2-$C_6H_4(CH_3)_2$	,,	0·631	−0·784	0·064	29·7	1·0	6	$25·1_5$
20	1 : 3-$C_6H_4(CH_3)_2$	,,	0·266	−0·763	0·043	14·5	1·6	6	13·0
25	1 : 4-$C_6H_4(CH_3)_2$	,,	0·193	−0·770	0·052	11·7	4·1	6	10·6
25	1 : 4-$C_6H_4Cl_2$	,,	0·310	−0·190	0·098	34·1	4·6	6	38·6
20	1 : 4-$C_6H_4Br_2$	,,	0·250	0·201	0·086	21·9	4·9	6	40·3
20	1 : 3 : 5-$C_6H_3(CH_3)_3$	,,	0·165	−0·840	0·004	9·28	2·8	6	10·1
20	1 : 3 : 5-$C_6H_3Cl_3$	,,	0·404	−0·122	0·079	26·4	3·2	5	37·6
20	1 : 3 : 5-$C_6H_3Br_3$	,,	0·324	0·317	0·084	9·69	6·6	6	24·3
25	1 : 3 : 5-$C_6H_3(NO_2)_3$	C_6H_6	0·391	0·472 †	0·039 †	10·1	7·2	6	168
25	$C_6(CH_3)_6$	CCl_4	0·244	−0·695	0·125	11·7	6·8	7	16·0
20	C_6Cl_6	,,	0·315	$0·517_5$	0·049	4·43	0·2	6	103·6

* Recalc. from Le Fèvre and Le Fèvre, *J.*, 1953, 4041.
† Calc. from data of Le Fèvre and Le Fèvre, *J.*, 1935, 957.

Molar Kerr constants for eight of the above solutes in carbon tetrachloride are to be found in the literature. The earlier values given for benzene, chlorobenzene, and nitrobenzene are quoted in our previous paper, those for the remaining five substances are noted here (all determined at 4° with light of $\lambda = 5461$ Å):

CH_3Cl	$40·8 \times 10^{-12}$	(Sachsse, *Physikal. Z.*, 1935, **36**, 360)
C_2Cl_6	$4·9 \times 10^{-12}$	(*idem*, *ibid.*)
C_6H_5Br	182×10^{-12}	(Otterbein, *ibid.*, 1933, **34**, 646)
C_6H_5I	183×10^{-12}	(*idem*, *ibid.*)
1 : 2-$C_6H_4Cl_2$	22×10^{-12}	(*idem*, *ibid.*)

Since neither Sachsse nor Otterbein gives B versus concentration figures, we are unable to check the extrapolations of $_mK_2$ to infinite dilution; presumably they evaluated $_mK_2$ for each individual solution—as did Briegleb, Friedrichs, *et al.* (see Le Fèvre and Le Fèvre, *J.*, 1953, 4041, for references)—and then attempted graphical extrapolation. From our experience we suspect the main cause of differences from the results on the right of Table 10 to lie in this procedure.

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SCHOOL OF CHEMISTRY, UNIVERSITY OF SYDNEY,
N.S.W., AUSTRALIA.

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The Triplet–Triplet Absorption Spectra of Some Aromatic Hydrocarbons and Related Substances.

By D. P. Craig and I. G. Ross.

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The absorption spectra of molecules, excited to the metastable lowest triplet state by irradiation of dilute rigid solutions, have been measured by means of a single-beam recording spectrophotometer. The extreme spectral range studied was from 7500 to 2650 Å or to the onset of ordinary electronic absorption. Triplet–triplet spectra are given, plotted on an arbitrary extinction scale, for naphthalene, fluorene, and 7 larger hydrocarbons, and the assignment of the bands observed is discussed. However, the expected $^3E_{2g} \longleftarrow {}^3B_{1u}$ transition in benzene was not detected, nor could the corresponding absorption be found in four related compounds. Spectra are also given for quinoline and *iso*quinoline, together with observations on some larger mono-nitrogen heterocyclics in which there is evidence of photolysis, especially in solvents containing alcohol or ether; triplet absorption was not found in pyridine or acridine. Solvent effects in these spectra are illustrated.

From the rate of decay of triplet–triplet absorption, values of the triplet-state lifetime were found in substantial agreement with those found from the rate of decay of phosphorescence. The concentration of triplet molecules under the experimental conditions used was found, from observations on the ground-state population, to be very small (<5% conversion); this conflicts with McClure's conclusion (*J. Chem. Phys.*, 1951, **19**, 670) that under even milder irradiation, the bulk of the solute molecules are converted into the metastable state. (The remainder of McClure's investigations, where overlapped by the present work, is however confirmed.) Finally, an unusual effect encountered here, which is probably due to photodecomposition, was a marked diminution of triplet–triplet absorption intensity during prolonged continuous irradiation.

(1) The best obeyed of all the selection rules which govern electronic transitions in molecules composed of the lighter elements is the intercombination selection rule, which prohibits transitions between molecular states of different multiplicities. In the vast majority of organic molecules—namely, those which contain an even number of electrons and have ground states with zero total electron spin (singlet states)—the more conventional methods of spectroscopy can hence only provide information regarding the location and vibrational structure of excited *singlet* states. Nothing is revealed concerning the equally interesting triplet (or diradical) states, or, *a fortiori*, of states of higher multiplicity. Experimental access to these states was only made possible comparatively recently through the work of G. N. Lewis and his associates on the mechanism of the fluorescence and phosphorescence which most covalent molecules can be induced to show under suitable conditions. The essence of this work was the demonstration of the rôle played by triplet states in the deactivation of a molecule excited by light absorption, and in particular that phosphoresence, the long-lived emission of energy lower than that absorbed, was in fact emission from the lowest triplet state. The long lifetime of such emission and the extreme weakness of the corresponding singlet–triplet absorption is due to the improbability of the intercombination transition, as prescribed by the selection rule.

To prevent the excited molecule's losing its energy entirely by radiationless collisional and interaction processes, it is usually necessary to disperse the substance as a dilute solution in a rigid solvent; the best glasses from an optical point of view are mixtures of various organic solvents, frozen in liquid nitrogen. The processes known to participate in the luminescence phenomena which may be observed in such solutions are shown in Fig. 1 (cf. Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14) which refers specifically to naphthalene. The most significant feature of this scheme is the possibility of inter-system crossing between the first excited singlet state S' and the triplet state T. From T both radiative

and non-radiative (quenching) processes combine to return the molecule to the ground state S, the mean lifetime of the state T being in this case 2·6 sec. While the molecule is in the state T it may be regarded as a distinct, if metastable, molecular species, having physical properties of its own. In particular, it should be possible to excite the molecule, by passing light of suitable wave-length, to higher triplet states T', T'', . . . (Fig. 1, process 6). This possibility was realized at the very beginning of the systematic investigation of the phosphorescence of organic molecules, by Lewis, Lipkin, and Magel (*J. Amer. Chem. Soc.*, 1941, **63**, 3005), who measured the triplet–triplet (T–T) absorption spectrum of fluorescein. Lewis and Lipkin (*ibid.*, 1942, **64**, 2801) made measurements on diphenylamine, and Grubb and Kistiakowsky (*ibid.*, 1950, **72**, 419) on certain dianthrones. McClure (*J. Chem. Phys.*, 1951, **19**, 670) reported on the first systematic investigation of the T–T spectra of 14 hydrocarbons and related molecules. Our work, which was initiated before Dr. McClure's publication, has been greatly assisted by it. Where the results overlap there is generally good agreement; we have extended the range of compounds examined, located

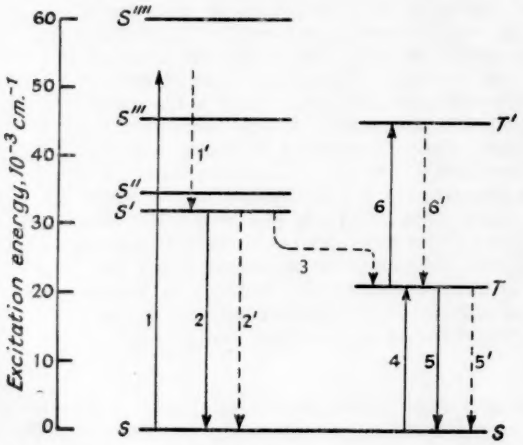


FIG. 1. Known radiative (full lines) and radiationless (broken lines) processes in naphthalene. **1**, Excitation to S', S''', . . .; **1'**, rapid internal conversion from S'', . . . to S'; **2**, fluorescence; **2'**, fluorescence quenching; **3**, inter-system crossing; **4**, (weak) singlet–triplet excitation; **5**, phosphorescence; **5'**, phosphorescence quenching; **6**, triplet–triplet absorption; **6'**, internal conversion to T.

additional bands in some of McClure's compounds, and obtained more precise estimates of T–T intensities.

(2.1) *Detection and Measurement of Triplet–Triplet Absorption.*—Consideration of Fig. 1 suggests that a triplet–triplet spectrum should be found by measuring the absorption spectrum of a solution in which a steady triplet-state concentration is maintained by simultaneous intense irradiation in the region of ordinary (singlet–singlet, or S–S) absorption. Success in detecting the triplet spectrum will depend, *inter alia*, on the number of triplet molecules which it is possible to generate in the light path. A favourable arrangement therefore is to pass the measuring beam along the axis of a cylinder of rigid solution, which is subjected to crosswise irradiation along its length (cf. Fig. 2). If it is assumed that the molecule has a sufficiently intense T–T absorption in the accessible wave-length range [2600—7500 Å; see (5·3), p. 1603] there are a number of conditions that limit the observation of the spectra. These are listed below and discussed in following sections: (i) A total number of triplet molecules must be maintained sufficient to give measurable absorption. (ii) The triplet molecules must be distributed in the solution so that the spectrophotometer light beam is effectively intercepted. (iii) The T–T bands must not be masked by S–S bands in the same region. The usually overwhelming preponderance of singlet molecules will, in this case, make detection of T–T absorption impossible.

(i) and (ii) both affect the degree to which the illumination from the spectrophotometer source is absorbed by the triplet molecules. For a given distribution of triplet molecules, the absorption is proportional to their number; hence it is important to make this as large as possible by having an intense exciting source and by using high concentrations; intense

exciting sources are readily available for substances which absorb at wave-lengths longer than 2500 Å. The effect of concentration in the apparatus of Fig. 2 is, however, complicated by the fact that, with lateral excitation, the triplet molecules are concentrated in the outer regions of the solution. In a too concentrated solution the triplets form in a thin cylindrical annulus in the outermost zone, and therefore present to the spectrophotometer a narrow ring of high optical density surrounding a circular area containing almost no triplet molecules : the apparent average optical density in such a case is thus almost zero. The selection of the most suitable concentration for the solution is thus an important question, and is referred to again in (2.3).

Apart from these controllable factors, high percentage conversions into the triplet state are favoured by long triplet lifetimes and high probabilities of inter-system crossing (Fig. 1,

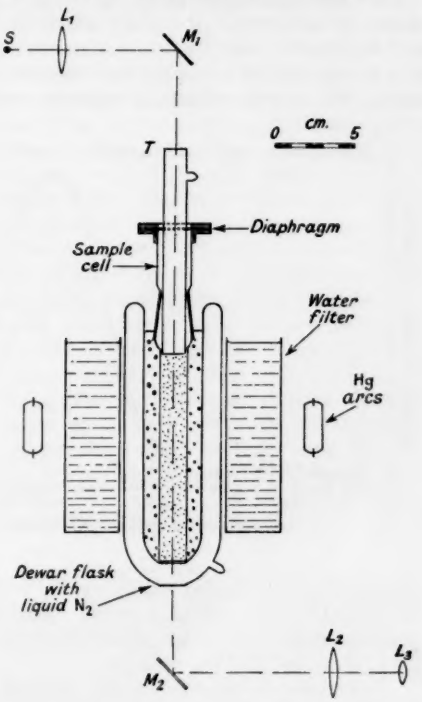


FIG. 2. Apparatus for the measurement of triplet–triplet absorption. *S*, light source; L_1, L_2, silica collimating and focusing lenses; L_3, entrance lens of Cary spectrophotometer; M_1, M_2, front-aluminized mirrors; *T*, evacuated tube.

process 3) compared to fluorescence and fluorescence quenching (processes 2 and 2′). Many triplet lifetimes are known but an *a priori* assessment of these other factors usually requires a knowledge of the ratio of luminescence mechanisms more detailed than is at present available.

(2.2) *Apparent Optical Density and Extinction Coefficient for Triplet–Triplet Absorption.*—For an absorbing system of non-uniform optical density, the measured density (the light-sensitive element being assumed faithfully to integrate the input energy) is the apparent optical density, ρ_A. We define this to be $\rho_A = -\log_{10} I/I_0$, where I is the total light flux emerging from the specimen, and I_0 the incident flux. If the mean concentration of triplet molecule is c_t, then we arrive at the apparent extinction coefficient ε_A : $\rho_A = \varepsilon_A c_t l$, l being the cell length in cm. In our experiments we have not directly measured c_t. We shall, however, infer an upper limit to c_t in various ways, the corresponding ε_A being then a lower limit to the apparent extinction coefficient for triplet–triplet absorption.

(2.3) *Selection of Concentrations of Solutions.*—The rôle of solute concentration in determining the intensity of triplet–triplet absorption has been described in (2.1), and the

selection of the optimum concentration is of obvious importance. Moreover, the distribution of absorbing molecules across the path of the measuring light being non-uniform, apparent and true extinction coefficients are not the same, nor will the ratio of two apparent extinction coefficients be the same as the ratio of the two corresponding true extinction coefficients. However, if the non-uniformity of the triplet distribution is not too great, the difference between such ratios will be very small. Under such conditions, then, even when the mean triplet concentrations are left undetermined, a plot of apparent optical densities against wave-length will differ from a plot of true extinction coefficients only by a constant scale factor. It is important then to use concentrations for which the differences between true and apparent optical densities are minimal, compatibly with the triplet–triplet absorption's being sufficiently intensely developed.

The formal analysis of this question is given by one of us elsewhere (Ross, *J. Opt. Soc. Amer.*, in the press). It is there shown that, with the experimental arrangement used here and with monochromatic irradiation, the apparent optical density of triplet–triplet absorption is a maximum when the optical density for the exciting wave-length is approximately unity; the corresponding concentration may be called the "optimum" concentration. A

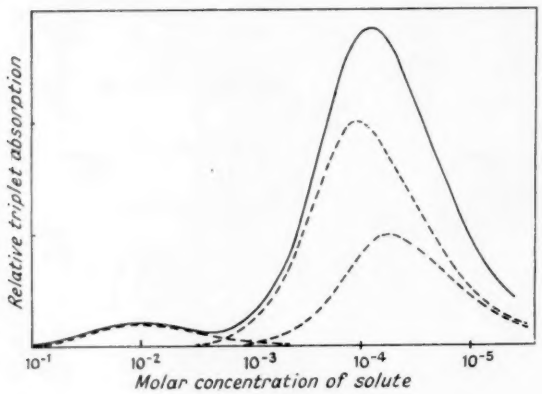


FIG. 3. Relative intensity of triplet–triplet absorption as a function of solute concentration, calculated for a hypothetical solute with three-line exciting source. The broken curves are the contributions to the absorption intensity due to the separate lines, the full curve is their sum. The rigid solution was taken to be in the form of a plane slab, 1 cm. thick, normally and uniformly irradiated from both sides.

change in concentration either way by a factor of 2 does not greatly decrease the intensity of excitation-induced absorption. Finally, apparent optical densities are very nearly proportional to true extinction coefficients (for triplet absorption) at solute concentrations up to about 80% of the optimum.

It remains to consider briefly the case of irradiation by non-monochromatic light. A specific, hypothetical, example will serve. Suppose the sample is simultaneously irradiated at wave-lengths λ_1, λ_2, λ_3, the relative intensities of these lines being I_1, I_2, I_3, and the extinction coefficients of the solute for the three wave-lengths ε_1, ε_2, ε_3. Now, for monochromatic irradiation (λ_1 alone, say), if the calculated triplet optical density, for measuring light of a given wave-length λ, is plotted against the logarithm of solute concentration, a bell-shaped curve is obtained with the maximum at the optimum concentration for the exciting line.

The height of this maximum is approximately equal to the product $kI_1\varepsilon_t(\lambda)$, $= \beta$ say; the factor k may be taken as being proportional to the triplet-state lifetime. The optimum concentration for simultaneous irradiation at three wave-lengths can then be predicted by adding together three such curves, one for each exciting line. Thus, suppose $I_1 : I_2 : I_3 = 2 : 2 : 1$, that $\varepsilon_1 = 10^{-2}$, $\varepsilon_2 = 10^{-4}$, $\varepsilon_3 = 5 \times 10^{-5}$, and the thickness of the sample is 1 cm. The factor k is virtually constant at low concentrations but falls off in concentrated solutions owing to self-quenching; hence we may take, in this illustration, $k_1 : k_2 : k_3 = 1 : 10 : 10$. Then $\beta_1 : \beta_2 : \beta_3 = 2 : 20 : 10$.

The three curves, and their sum, calculated for this particular situation, are shown in

Fig. 3. It is seen that the optimum concentration is determined very largely by the intense line, but that the maximum of the intensity curve is even flatter than when monochromatic radiation is used. This is clearly a general result, and may be extended to cover irradiation by a many-line or a continuous source, and the optimum concentrations may be calculated, given the source characteristics and the absorption spectrum of the solute. Mostly this information will *not* be available, but it is clear that a concentration unimportantly different from the optimum will have been used if a series of solutions are examined whose concentrations differ from each other by a factor of about four.*

In the present work triplet–triplet spectra were sought in this fashion, and the intensity of triplet absorption, when found at all, was indeed observed to vary with concentration roughly as predicted here.

(3.1) *Apparatus and Accuracy of Results.*—Fig. 2 illustrates the apparatus and method of measurement of T–T spectra. A full description is given in (5.1). The apparatus differs from that of McClure in some small but important respects; but in principle it is the same. We recorded the focused light beam after its passage through the frozen sample on a Cary Recording Spectrophotometer. The traces are compared with spectra taken without excitation and with others taken with excitation but without source illumination. The apparent optical density curves shown hereafter are constructed from such sets of three traces. The reproducibility of traces was, in all cases upon which our results are based, better than 5% and rarely worse than 2%. Uniform drifts caused deviations of this kind, due to voltage fluctuations which were ultimately eliminated; or to softening of the glassy solutions by the absorbed light, which appears to be an intrinsic difficulty. Wave-lengths have a probable error not greater than 5 Å, although the maxima of broad peaks are not known so precisely as this. The relative extinction coefficients involve many uncertainties, but comparison of spectra calculated from different experiments with the one substance suggest that, for spectra which were intensely developed (maximum optical density >1), errors in the relative extinction coefficient should not exceed 0·05 unit. The error should vary smoothly with wave-length, so that the shape of a curve is more reliable than the quoted error suggests. Exceptions to this statement are marked in the spectra by dotted lines. Here there are special disturbing factors making precise measurement difficult, such as strong sample fluorescence, discontinuity in the source spectrum, or S–S absorption showing structure. Mercury lines occur, as shown in the spectra, by scattering of the exciting light. The spectra are interpolated in these regions, which are usually so narrow that the error introduced is insignificant.

(3.2) *Choice of Rigid Solvents.*—Triplet–triplet absorption spectra were measured in two kinds of glass, consisting of mixed solvents frozen in liquid nitrogen. The mixtures are denoted as EPA (ether–*iso*pentane–alcohol) and PMh (*iso*pentane–methyl*cyclo*hexane).

Triplet spectra measured in the two solvents are not often materially different, there being only a modest wave-length displacement, and perhaps slight modification of the vibrational structure. In other cases, however, there is an important effect. Thus Lewis and Lipkin (*loc. cit.*) as mentioned in (1), found excitation-induced absorption in diphenylamine, our measurement of which is shown in Fig. 4; it is extremely intense, and can be obtained with quite feeble irradiation, the solution turning deep red-purple. Yet in PMh we were unable to find any sign of triplet–triplet absorption. In EPA, however, irradiation of diphenylamine induces a complex series of photoreactions, as Lewis and Lipkin discussed, and the solution after irradiation is found to have acquired a green colour which is permanent as long as the solution remains frozen. It seems likely that the excitation-induced absorption is not due, as Lewis and Lipkin supposed, to diphenylamine itself, but to the green substance, which they concluded was the ion $[(C_6H_5)_2NH]^+$ produced by photo-ejection of an electron. In PMh solution, where there is no potential electron-acceptor present, such photo-oxidation does not occur, and no green coloration is found. No photo-oxidation was detected in any of the hydrocarbons studied, or in the smaller hetero-aromatic compounds. The angular benzoquinolines and benzacridines gave definite evidence,

* This discussion assumes (*a*) that the ground state is not significantly depopulated [cf. (4.1)] and (*b*) that the exciting wave-lengths are not absorbed by the triplet molecules. In the former case the optimum concentration is higher, but even less critical, than that predicted here; in the latter it is lower.

however, of such an effect in EPA solutions, and with such molecules it appears essential that triplet spectra be measured with hydrocarbon solvents.

(3.3) *Results.*—The spectra measured in this way are shown in Figs. 4—7. The numeri-

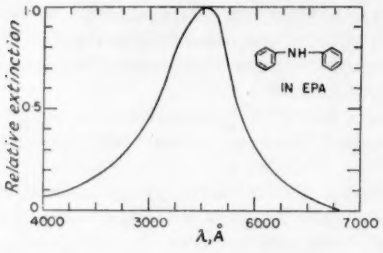
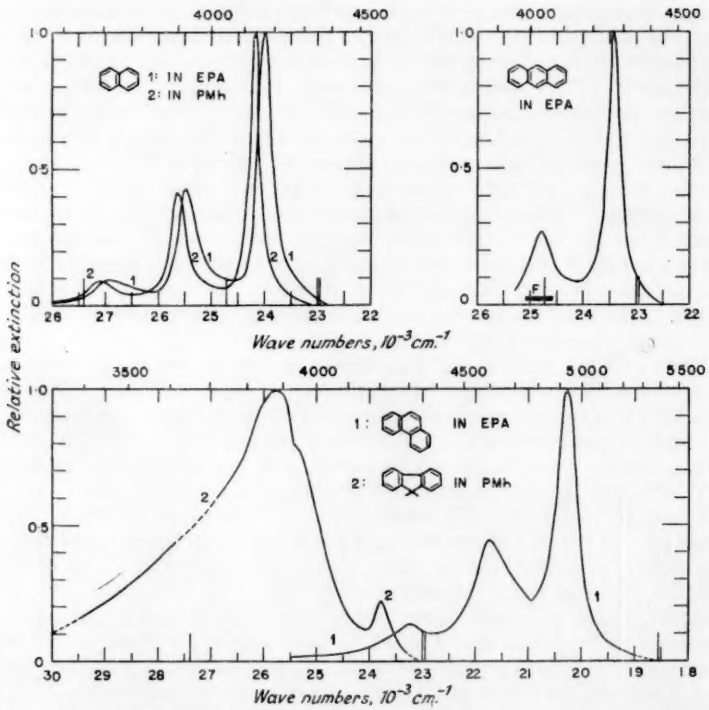


FIG. 4. Irradiation-induced absorption of diphenylamine in ether–*iso*pentane–alcohol (EPA) at 77° K.

cal values are in Tables 1 and 3, and the properties of the triplet levels are given in Table 2. The relative intensities of absorption maxima shown in the Figures and Tables and denoted by $\rho_{rel.}$ are the extinctions relative to the most intense observed band; they also denote, subject to the considerations discussed in (2.3), ratios of extinction coefficients.

FIG. 5.



Triplet–triplet absorption spectra of naphthalene, anthracene, phenanthrene, and fluorene. Temperature 77° K. Curves are broken where their accuracy is reduced. Long vertical lines along the bases of the figures show the positions of mercury lines. Solid bars above the base lines indicate the location of simple fluorescence (*F*) and ordinary absorption (*A*), when present.

The data in the frequency column of Table 1 overlap the results of McClure (*loc. cit.*) in part, and the agreement throughout is good. The intensity of excitation was greater than McClure's, which, together with our ability to distinguish bands overlaid by sample

luminescence, accounts for the additional peaks found. McClure recorded two measurements of relative extinction coefficient : he found 0·45 (present work 0·43) for the second peak of naphthalene, and 0·56 (present work 0·45) for the second peak of phenanthrene. In the latter case his result lies outside the probable error of our measurement.

TABLE 1. *Characteristics of observed triplet–triplet absorption spectra.*

Obs. triplet bands cm.$^{-1}$	$\rho_{rel.}$
Naphthalene in EPA	
*24,000 ± 25	1·00
*25,465 ± 30	0·43
26,950 ± 100	0·10
Naphthalene in PMh	
24,185 ± 25	1·00
25,675 ± 30	0·41
27,175 ± 150	0·09
Anthracene in EPA	
*23,420 ± 30	1·00
24,750 ± 50	0·27
Phenanthrene in EPA	
*20,280 ± 30	1·00
*21,730 ± 50	0·45
23,200 ± 50	0·14
Fluorene in PMh	
23,750 ± 50	0·23
25,300 ± 100	S
25,800 ± 100	1·00

Obs. triplet bands cm.$^{-1}$	$\rho_{rel.}$
Chrysene in EPA	
*15,900 ± 100	0·11
17,150 ± 50	1·00
17,750 ± 150	S
18,500 ± 150	S
24,630 ± 150	0·18
26,000 ± 250	0·15
1 : 2-*Benzanthracene in EPA*	
*20,450 ± 20	1·00
*21,100 ± 100	S
*21,700 ± 75	0·58
23,050 ± 100	0·54
1 : 2-*Benzanthracene in PMh*	
20,550 ± 20	1·00
21,200 ± 100	S
21,800 ± 100	0·62
23,250 ± 150	0·55

Obs. triplet bands cm.$^{-1}$	$\rho_{rel.}$
1 : 2-5 : 6-*Dibenzanthracene in EPA*	
*17,100 ± 30	1·00
*18,280 ± 30	0·67
*19,700 ± 100	0·39
*20,000 ± 100	0·40
21,200 ± 150	0·30
23,350 ± 150	0·24
Pyrene in EPA	
19,050 ± 100	0·20
19,400 ± 100	S
20,450 ± 100	0·15
24,070 ± 30	1·00
26,900 ± 200	0·10
3 : 4-*Benzopyrene in EPA*	
19,850 ± 100	0·31
20,950 ± 50	0·95
21,370 ± 50	1·00
22,500 ± 100	0·76

Obs. triplet bands cm.$^{-1}$	$\rho_{rel.}$
Quinoline in EPA	
20,550 ± 100	0·40
21,050 ± 100	S
21,850 ± 100	0·59
23,400 ± 200	0·98
24,850 ± 300	1·00
~26,300	S
Quinoline in PMh	
(19,000	0·04)
20,600 ± 150	0·22
22,200 ± 150	0·42
23,800 ± 150	0·97
25,300 ± 150	1·00
~26,800	S
iso*Quinoline in EPA*	
20,500 ± 200	0·03
21,800 ± 200	0·09
23,720 ± 50	1·00
25,000 ± 250	0·66
iso*Quinoline in PMh*	
24,150 ± 50	1·00
25,500 ± 150	0·50

S denotes an unresolved shoulder. * Position of band also recorded by McClure (*loc. cit.*).

TABLE 2. *Collected data on triplet states.*

Compound	Lowest triplet (cm.$^{-1}$) [a]	Excited triplets (cm.$^{-1}$) [b]	Max. obs. ρ_A [c]	Lifetime τ_P^0 (sec.) [d]	Triplet colour
Naphthalene	21,300	45,000	>1	2·5 ± 0·1	Yellow
Anthracene	14,700	38,120	1	<0·1	—
Phenanthrene	21,600	41,880	>1	3·3 ± 0·2	Yellow
Fluorene	23,750	47,500	1	5·7 ± 0·3	Yellow
Chrysene	19,800	35,700	⩾1	2·6 ± 0·2	Red
		44,430			
1 : 2-Benzanthracene	16,500	36,950	⩾1	0·3 ± 0·1	Yellow
1 : 2-5 : 6-Dibenzanthracene	18,300	35,400	⩾1	1·4 ± 0·1	Red-purple
Pyrene	16,800	35,850	0·4	0·7 ± 0·2	Yellow
		40,870			
3 : 4-Benzopyrene	—	—	0·3	<0·1	Yellow
Quinoline	21,700	42,250	0·3	0·5 ± 0·2	Yellow
*iso*Quinoline	—	—	0·3	1·3 ± 0·3	Yellow

[a] McClure, *J. Chem. Phys.*, 1949, **17**, 905. [b] *I.e.*, total energies calculated from apparent origins of triplet–triplet transitions. [c] Optical densities of strongest bands under maximum available excitation. [d] Measured from rate of decay of triplet absorption.

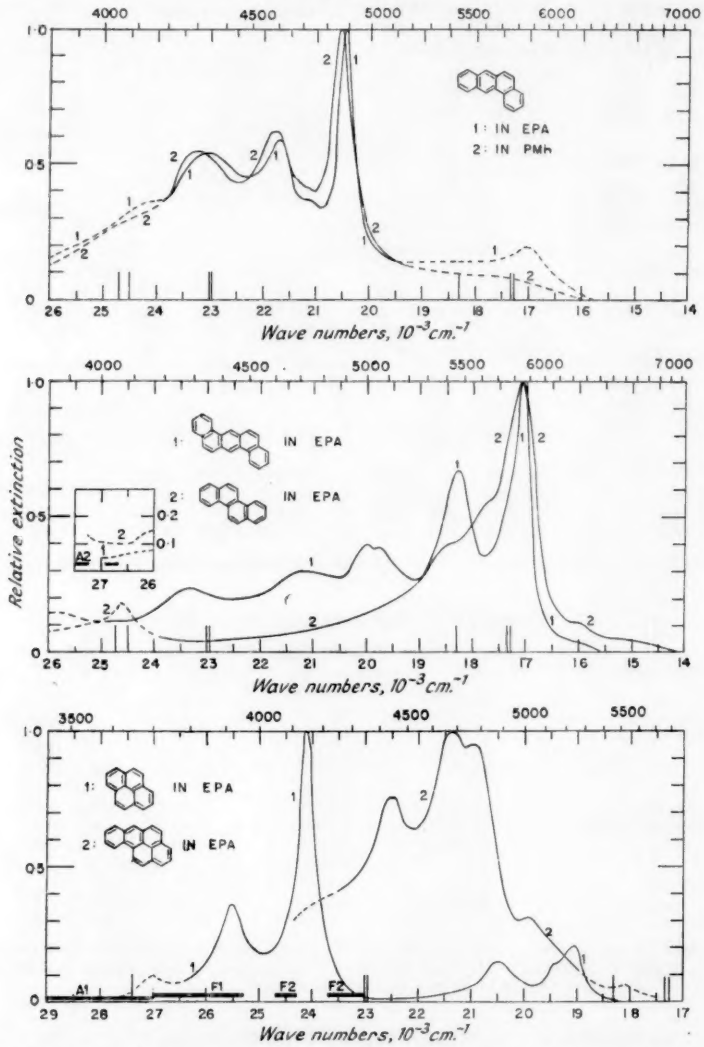
Tables 2 and 3 contain, as well as quantitative information, a list of the colours of the triplet states. These colours are visible along the length of the irradiated cell, and are a striking feature of the experiments.

(3.4) *Naphthalene, Anthracene, and Phenanthrene.*—Discussion of the negative result in benzene being deferred, we deal with the three simplest aromatic hydrocarbons first. They show very similar, and simple, spectra. Naphthalene and phenanthrene give stronger spectra than anthracene, probably because the last emits absorbed light very efficiently as fluorescence, and also has a short-lived triplet state. The band groups appearing as peaks

are all distinctly narrow (300—500 cm.$^{-1}$), and complex structure as found in other molecules is missing. The peaks fall into progressions with spacings approximately:

Naphthalene: 1490, 1500 cm.$^{-1}$ (in PMh); 1465, 1515 cm.$^{-1}$ (in EPA)
Anthracene: 1330 cm.$^{-1}$ (EPA)
Phenanthrene: 1450, 1470 cm.$^{-1}$ (EPA)

FIG. 6.

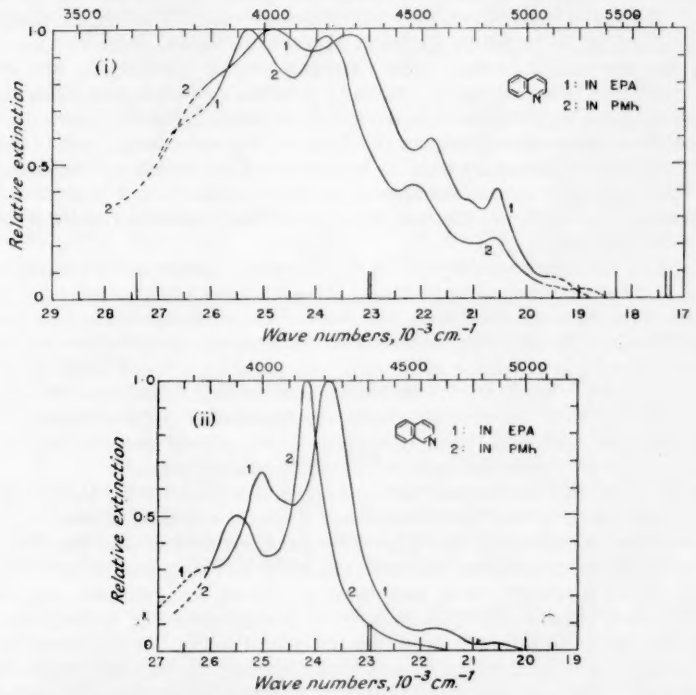


Triplet–triplet absorption spectra of 1 : 2-benzanthracene; 1 : 2 : 5 : 6-dibenzanthracene and chrysene; and of pyrene and 3 : 4-benzopyrene. See also notes to Fig. 5.

These frequencies are close to totally symmetric frequencies of about 1400 cm.$^{-1}$ which are a prominent feature of the singlet spectra of these and many other condensed hydrocarbons, and we may assume that similar vibrational modes are involved. These modes involve principally the carbon skeleton (Dr. H. McConnell, personal communication) though their precise nature, and the reason for their prominence, are not yet understood.

The intensity of the band systems must be measured indirectly. The method is described in (4.1); it allows a lower limit to be set to the extinction coefficients from an estimate of the upper limit of the triplet concentration. In naphthalene the extinction coefficient is not less than 10,000 and in anthracene not less than 50,000, leading to oscillator strengths not less than 0·05 and 0·25, respectively. These values, coupled with the simple vibrational pattern, suggest an allowed transition; and one polarized in the molecular plane. Now, powerful theoretical arguments indicate that the lowest triplet levels of naphthalene and anthracene belong to $^3B_{2u}$ of point group D_{2h}; allowed in-plane transitions from this state end at states belonging to $^3B_{1g}$ (long-axis polarized) or ^3A_g (short axis). In the alternative notation which Platt (*J. Chem. Phys.*, 1949, **17**, 484) has recently introduced for use

FIG. 7.



Triplet–triplet absorption spectra of quinoline and *iso*quinoline. See also notes to Fig. 5.

with condensed aromatic molecules, these two possibilities would be described as (^3K_a or ^3K_b) ← ^3L_a. Experimental evidence does not yet allow a choice to be made between these two. We do, however, believe that McClure's assignment to a forbidden transition is untenable in view of the intensities mentioned above and discussed in (4.1).

(3.5) *Fluorene.*—Compounds with less than two fused benzene rings, have not, with this one exception, so far yielded *T*–*T* spectra. Fluorene gives a poorly resolved spectrum, almost certainly with less structure than the *S*–*S* spectrum would show at equally low temperatures.

(3.6) *Larger Condensed Hydrocarbons.*—The triplet absorption of the benzanthracenes and chrysene are very intense, and are developed sufficiently for measurement with only about one-tenth of the irradiation intensity necessary for the 2- and 3-ring hydrocarbons. These spectra show considerable vibrational structure with, at the same time, insufficient regularity in the band-spacings to justify attempting vibrational analyses. In the benzanthracenes, the principle bands are well resolved, but in chrysene the resolution is

surprisingly poor, the difference being enough to suggest that the transitions belong to different series, in Platt's sense (*loc. cit.*). Chrysene is further distinguished by showing in the region examined two electronic transitions, the second occurring around 25,000 cm.$^{-1}$ with about one-fifth of the intensity of the first. This transition overlaps the intense singlet-absorption spectrum and is overlaid by two strong mercury lines; the measurements here are therefore somewhat qualitative, although the existence of the new transition is definite.

It is necessary to comment on our spectra of 1 : 2-benzanthracene. To the long-wave-length side of the principal absorption band there was found in EPA solution another band at 17,000 cm.$^{-1}$; in PMh there was marked absorption with no positive maximum. No absorption in this region was reported by McClure. In our measurements, absorption in this region was observed to decay at about one-quarter of the rate of the rest of the spectrum [cf. (3·9)], and is consequently rejected as spurious. Whether it is due to a photo-oxidation product or to impurity (possibly dibenzanthracene, from the nature of this absorption) we are unable to say. The chromatographic purification was reported as " difficult " but this absorption was the same both before and after such refinement.

Chrysene and possibly dibenzanthracene are distinguished from the previous compounds by showing at least one weak vibrational band on the long-wave-length side of the strongest peak. These bands are unusually weak to be accounted for simply by the Franck–Condon effect, but the transitions themselves appear to be so intense that it is most unlikely that the long-wave-length bands are the origins of forbidden transitions made feebly allowed by solvent perturbations.

In contrast to the intense absorption of the three cata-condensed hydrocarbons above, pyrene and 3 : 4-benzopyrene absorbed only comparatively weakly under full irradiation. Pyrene shows two distinct absorption systems which must correspond to two distinct upper triplet levels. The principal bands in each system are spaced at around 1400 cm.$^{-1}$, and in view of the high molecular symmetry this could be a single predominant totally-symmetric frequency. Again, the lowest energy band in each transition is the most intense. It is not surprising that the comparatively unsymmetrical benzopyrene should show a completely different spectrum with no apparent vibrational progression and reaching maximum intensity only with the third or fourth vibrational band.

In none of these five compounds do we suggest assignments for the electronic levels concerned, except to note that the transitions are almost certainly allowed.

(3.7) *Quinoline,* iso*Quinoline, and Other Nitrogen Heterocycles.*—No spectra were found in pyridine [see (3.8)] or acridine, but both quinoline and *iso*quinoline gave weak absorption. These differ markedly from naphthalene, having an extended series of poorly resolved vibrational bands. The spectra differ somewhat according as they were measured in EPA or PMh solutions, but in interpreting the curves of Fig. 7 it is to be recognized that these spectra were weakly developed, and that errors in the intensity scale could be as large as 0·2 unit. For this reason the failure to find in PMh solutions of *iso*quinoline the long-wave-length bands just detectable in EPA is not proof positive of their non-existence, while in the spectrum of quinoline in EPA it would be premature to speculate on the curious structure in the region 20,000—21,000 cm.$^{-1}$. A definite effect of change of solvent, however, is a blue shift in each case of about 400 cm.$^{-1}$ on passing fron EPA to PMh; there is no evidence of photolysis in solutions in EPA.

Allowance being made for the difficulty in locating the band maxima, it appears that both quinolines show long progressions in a single frequency of about 1400 cm.$^{-1}$, about the same as the only frequency observed in naphthalene. Compared with those of naphthalene, the maxima are shifted slightly towards long wave-lengths, but the first band is no longer the strongest. This change is much more marked in the α-hetero-molecule, quinoline, than in the β-isomer. Presumably at the comparatively high energy of the upper triplet state (total about 41,000 cm.$^{-1}$) the unbound electrons of nitrogen are interacting significantly with the π-system. This interaction might be expected to manifest itself also in the ordinary singlet absorption to levels of the same or higher energy, but although the singlet spectra of the two quinolines show less structure in the 2500 Å region than does naphthalene, the required measurements at low temperatures have not been made.

With the four non-linear benzoquinolines and benzacridines, photoreactions occur in EPA, and irradiation-induced absorption is greater in that solvent than in PMh. All absorption bands, in either solvent, were no better resolved than those of quinoline. We record in Table 3, as preliminary results only, the features of the observed spectra; the lifetime measurements in that Table were determined from the rate of decay of absorption.

TABLE 3. *Triplet–triplet absorption of* N-*heterocyclics.*[a]

Solute	Solvent	Intensity of absorption	Absorption maxima (Å)	$\rho_{rel.}$	τ_P^0 (sec.)	Remarks
7 : 8-Benzoquinoline	PMh	Weak	5050	1·0	1·4	—
			~4650	0·9		
	EPA	V. strong	5000	1·0	2·1	Colour during irradiation deep orange. Permanent change suspected
			4650	0·8		
			~4400	0·5		
5 : 6-Benzoquinoline	PMh	Weak	5100	1·0	1·8	—
	EPA	V. strong	5170	1·0	2·6	Colour during irradiation deep orange; after irradiation, permanently pink, bands at 5600 and 5100 Å
			4820	0·8		
			~4520	0·5		
1 : 2-Benzacridine	PMh	V. weak	4970	1·0	<0·5	—
	EPA	V. strong	4970	1·0	0·3	Colour during irradiation deep orange; afterwards solution showed one very weak permanent absorption band at 4270 Å
			4700	0·9		
3 : 4-Benzacridine	PMh	None	—	—	—	—
	EPA	Moderate	5100	1·0	0·4	Colour during irradiation yellow. No evidence of permanent change
			4800	0·9		

[a] All solutions of approx. concentration 2×10^{-4}M. Spectra examined from 7000 Å to the onset of ordinary absorption around 4000 Å. Below 4300 Å most records showed intense fluorescence. All absorption bands detected were very broad, and in most cases absorption extended over most of the spectral range examined.

(3.8) *Benzene and Other Monocyclic Compounds.*—*T*–*T* absorption was sought, under widely varying conditions, in solution of benzene, hexamethylbenzene, diphenyl, diphenylamine, and pyridine. With use of the " Pointolite " hot tungsten light source, solutions of each substance were scanned between 7500 and 3050 Å; benzene and pyridine were further examined between 3500 and 2650 Å, the carbon arc being used. In no case was *T*–*T* absorption by these molecules found. The absorption in EPA solutions of diphenylamine is considered to be due to a photochemically derived substance [see (3.3)]. These negative results, added to those of McClure (*loc. cit.*) for aniline and phenol, call for some discussion.

Every theoretical and analogical consideration suggests that there should be at least one absorption band, and probably more, in the spectral region examined. Specifically a non-empirical calculation of the energy levels of benzene by Parr, Craig, and Ross (*J. Chem. Phys.*, 1950, **18**, 1561) predicts an allowed in-plane $^3E_{2g} - {}^3B_{1u}$ transition at 18,500 cm.$^{-1}$. Forbidden bands are predicted at 5000 and 33,000 cm.$^{-1}$. The precision of these calculations is not great—comparison with available experiment shows up errors of as much as +15,000 cm.$^{-1}$—but in these cases there are definite reasons why the calculated levels should be too high (they are levels whose wave functions, in the language of the valence-bond theory, are expressible only in terms of polar structures—cf. Craig, *Discuss. Faraday Soc.*, 1950, **9**, 5); these considerations do not apply to either the $^3B_{1u}$ or $^3E_{2g}$ levels. Moreover, and probably more convincingly, the existence of transitions at 24,000 and 23,420 cm.$^{-1}$ in naphthalene and anthracene naturally suggests that there should be a triplet transition around 25,000—30,000 cm.$^{-1}$ in benzene.

Failure to detect absorption bands may result from too low a concentration of triplet molecules, or intrinsic weakness in the bands themselves. A forbidden *T*–*T* absorption of about the same strength as the benzene *S*–*S* system at 2600 Å might well escape detection. In naphthalene we obtained a *T*–*T* optical density of 1·0 in an allowed transition by intense irradiation of a 0·0004M-solution. An optical density of about one-fiftieth of this was detectable in our experiments, so that with an equal concentration of benzene triplets a transition less than one-fiftieth of the naphthalene strength might have escaped detection.

In the singlet series the ratio of forbidden to allowed intensities is usually 1/100 or less, so that from considerations of oscillator strength the possibilities are marginal. On the other hand, if the transition in benzene is allowed then its non-appearance must be due to too low a steady concentration of triplet molecules.

This question of the steady concentration of triplet molecules has been analysed by McClure (*loc. cit.*) in terms of the processes depicted in Fig. 1, for cases in which there is no photochemical decomposition. Such an analysis was applied here, the data on triplet lifetimes, quantum yields of phosphorescence, and concentration quenching given by Gilmore, Gibson, and McClure (*J. Chem. Phys.*, 1952, **20**, 829) being used with appropriate data on the extinction coefficients for the exciting light. This led to the expectation that, possibly in benzene, and certainly in some of its derivatives, triplet concentrations should be achieved higher than were found with naphthalene.

The details of this argument we omit, since very recently Gibson, Blake, and Kahn (*ibid.*, 1953, **21**, 1000) have shown that under our experimental conditions, benzene is fairly rapidly decomposed to hexatriene by light of wave-length 2537 Å. This product is formed in the outer layers of the rigid solution, and its high extinction coefficient at 2537 Å would effectively filter out the exciting light and prevent the formation of triplets, or further hexatriene, within the bulk of the solution. This photoreaction, which may be related to some of our own observations on higher hydrocarbons [cf. (4.2)], could well account for the failure to find triplet–triplet absorption in benzene and its derivatives. The most reasonable alternative explanation for this failure is that the benzenoid compounds have strong triplet–triplet absorption at 2537 Å; the triplet molecules themselves would then absorb the exciting light.

(3.9) *Measurement of Phosphorescence Lifetimes.*—The mean lifetime of the triplet state (or observed phosphorescence lifetime, τ_P^0) has hitherto always been determined from measurement of the rate at which phosphorescence intensity decays after the cessation of irradiation. The decay is strictly of first order, and the reciprocal of the rate constant is the mean lifetime, as normally defined. Lifetimes can also be determined from the rate of decay of triplet–triplet absorption, again after the cessation of irradiation. The method is less general than the phosphorescence-decay technique, but is useful when the phosphorescence is particularly feeble or occurs in the infra-red where intensity measurements are difficult. This is so, for example, with anthracene, for which even the wave-length of the phosphorescence is not definitely known (cf. Reid, *ibid.*, 1952, **20**, 1214). Triplet-state lifetimes were here measured by setting the spectrophotometer at fixed wave-length, usually the peak of a triplet absorption band, and recording intensity as a function of time. During the course of the record, the lamps were switched off, and the intensity transmitted by the frozen solution rose to its limiting value corresponding to no triplet absorption. In calculating the decay constants due account was taken of the fluorescence and scattered light whose decay was instantaneous. It will be noticed that the method is valid even if singlet–singlet absorption is present and the ground state is measurably depopulated, since increase in the singlet absorption intensity will take place at precisely the same rate as that at which the triplet absorption decays. The accuracy obtainable by this method depends on the response of the recorder. The use here of a mechanical recorder meant that only mean lifetimes greater than 0·1 sec. could be distinguished from zero. The accuracy of the measurements determined from the constancy of the rate constants during the decay was at best of the same order.

For accurate measurements of this kind it is essential that triplet–triplet optical densities be as nearly as possible proportional to extinction coefficients. Because of the non-uniform distribution density to triplet molecules across the cell the relation between optical density and number of triplets is non-linear. Serious deviations from linearity will lead to rate constants for the decay which apparently increase with time. This was in fact observed in some solutions of concentration well above the " optimum " [the word being used in the sense defined in (2.3)], but mostly the calculated rate constants remained sensibly constant throughout the decay. Indeed, we have taken this observed constancy to justify the assumption of proportionality between optical density and extinction coefficients in the corresponding solutions.

The rate constants thus measured are included in Tables 2 and 3. In Table 2, seven of the deduced lifetimes can be compared with those measured by McClure (*ibid.*, 1949, **17**, 905), by the phosphorescence-decay method. Agreement is excellent, except for fluorene and pyrene for which McClure's figures are 4·9 ± 0·2 and *ca.* 0·2 sec., respectively. A decision between the values offered must await remeasurement, although possibly those found from phosphorescence decay, being subject to fewer complicating factors, are to be preferred. Of the remaining lifetimes given, that of anthracene is particularly interesting in view of the long lifetimes of benzene, naphthalene, and phenanthrene. The lifetimes of the heterocyclics confirm McClure's qualitative observation that such compounds appear to have the relatively long lifetimes characteristic of the parent hydrocarbons.

(4.1) T–T *Extinction Coefficients and the Concentration of Triplet Molecules.*—The steady concentration of solute molecules in their triplet states depends, *inter alia*, on the intensity of irradiation, and must be separately measured if the arbitrary intensity states of Figs. 4—7 are to be replaced by scales of extinction coefficients. McClure (*loc. cit.*) measured *T*–*T* optical densities as a function of excitation intensity and deduced the extinction coefficient by a relation, theoretically derived, between the reciprocal optical density and the reciprocal excitation-intensity. Values obtained by this method are, we believe, much too low.

Since population of the triplet state implies depopulation of the singlet state, the intensity of the *S*–*S* spectrum must diminish under conditions in which the *T*–*T* spectrum is observed. In principle, measurement of the intensity decrease in the *S*–*S* spectrum should give an accurate value of the population of the triplet state. In practice, under our conditions of excitation, the depopulation is undetectably small, so that only an upper limit can be given to it, and consequently only an upper limit assigned to the triplet concentration. The method is particularly simple for molecules having an *S*–*S* absorption system in a spectral region clear of *T*–*T* absorption. This occurs in naphthalene, for which we also have values of extinction coefficient at low temperature (Passerini and Ross, *J. Chem. Phys.*, in the press). At 3110 Å, the position of the 1 ← 0 band of the first singlet sytem, the extinction coefficient is about 400. A solution of naphthalene of concentration 0·0002M (calculated after allowance for contraction on freezing) gave a *T*–*T* optical density of 1·08 at its maximum at 4160 Å. At 3110 Å the *S*–*S* optical density was 0·8 and no difference in transmission could be detected with and without the excitation. Thus the number of molecules converted to give a *T*–*T* optical density of unity formed so small a fraction of the total as to remain undetected. A conservative estimate, allowing for the fact that not all of the cell was illuminated, is that not more than 5% of molecules were in the triplet state; the minimum value of the triplet extinction coefficient is 10,000. It is to be noted that the *T*–*T* optical density is an apparent density, in the sense of (2.2), and leads to a small extinction coefficient; for the same reason, that the singlets lost by depopulation are not uniformly spread across the cell, the *S*–*S* intensity change is *more* sensitive than expected on the basis of calculation we have used. We believe therefore that 10,000 for the *T*–*T* extinction is conservative to an extreme degree, and that this lower limit might be increased by at least a factor 2. In a similar study of phenanthrene the *T*–*T* optical density was 1·8 and no depopulation could be detected. A lower limit deduced as in naphthalene is 18,000. In anthracene a solution of $5{\cdot}9 \times 10^{-6}$M was examined in the same way. Its *T*–*T* optical density was 0·13. Its singlet spectrum showed no difference under excitation throughout the whole of the region 3850—3500 Å, which includes three strong maxima (3785, 3735, and 3595 Å). The extinction coefficient for *T*–*T* absorption at the 23,420 cm.$^{-1}$ maximum is not less than 45,000.

McClure's values for naphthalene, anthracene, and phenanthrene are 480, 2800, and 1560. In further support of our much higher values we refer briefly to two other lines of evidence. At low triplet concentrations, concentration increases almost linearly with increasing excitation, but falls off as saturation is approached. In a solution of anthracene $7{\cdot}8 \times 10^{-5}$M (run 1, Table 4) the optical densities at the wave-length of maximum absorption produced separately by three 125-w mercury lamps were 0·39, 0·41, and 0·25, all ±0·02. The sum of these figures is 1·05 ± 0·06. The three lamps operating simultaneously gave 1·02 ± 0·03 which, within experimental error, shows that the triplet con-

centration is still in the linear region of its dependence on excitation, implying the very low conversion of 1 or 2% at most. Finally, a number of EPA solutions of naphthalene and anthracene of steadily decreasing concentration were examined under the maximum available excitation. Considerable T–T absorption was shown by solutions so dilute that, even assuming ***complete*** conversion into triplet state, values of extinction coefficient are implied greater than those of McClure. These are summarised in Table 4. These lower limits are of course less than those in the penultimate line of Table 4 derived from depopulation measurements.

TABLE 4. *Lower limits to extinction coefficients of strongest triplet–triplet bands.*

Solute	Naphthalene		Anthracene		
Run No.	1	2	1	2	3
Concn. c (mole/l.)	$4{\cdot}4 \times 10^{-5}$	$2{\cdot}2 \times 10^{-5}$	$7{\cdot}8 \times 10^{-5}$	$2{\cdot}0 \times 10^{-5}$	$5{\cdot}9 \times 10^{-6}$
Irradiated path-length l (cm.)	5·0	5·0	6·0	5·0	5·5
T–T optical density ρ_A	0·90	0·70	1·20	0·31	0·13
Minimum extinction coeff., min. $\varepsilon = \rho_A/cl$	4000	6400	2200	3100	4000
Min. ε from ground-state depopulation	10,000			45,000	
ε (McClure, *loc. cit.*)	480			2,800	

(4.2) *The Slow Decrease in Triplet–Triplet Absorption under Continuous Irradiation.*—The estimates at which McClure, on the one hand, and the present authors, on the other, have arrived at the triplet state concentrations produced by irradiation of frozen solutions could hardly be more different.* The difference is far greater than can be accounted for by experimental errors, and can only be due to unsuspected complications in the two different methods used. The technique here of observing the ground-state population with and without excitation leads directly to an upper limit for the triplet concentration. McClure's method, outlined in (4.1), was much more inferential, and depended for its reliability on the transition scheme of Fig. 1 being complete and particularly on the absence of photodissociation, etc. Indeed, McClure was careful to point out that, in the event of such additional processes actually occurring his estimates of concentration and extinction coefficients could be greatly in error.

What the precise nature of these additional processes might be we do not understand at all fully. By far the most probable complication is photodecomposition, as referred to earlier (3.8) in connection with benzene. In the present work this was indicated especially in measurements on fluorene and naphthalene. The observations were in the nature of a slow but steady decrease in the overall intensity of triplet–triplet absorption under continued irradiation. The intensity of the singlet spectrum remained unaltered during the same experiments, showing that the effect of the irradiation, whatever its nature, did not permanently involve the bulk of the solute molecules in the measuring light-path.

We can illustrate this with a specific example. A naphthalene solution of concentration $1{\cdot}9 \times 10^{-4}$M was irradiated for a total of 95 min. Initially, the optical density of triplet absorption (strongest band) was 1·12; after 20 min. this had decreased to 0·38. With further irradiation the decrease continued, reaching apparently a limiting value of 0·25 (22% of the initial optical density) towards the end of the experiment. The rate of decrease of absorption intensity was approximately exponential. Interruption of the irradiation for periods up to 30 min. did not cause any recovery of the diminished absorption although our experimental technique did not allow the interesting experiment to be performed of melting and refreezing the glass to see whether the diminished absorption was then restored.

With more dilute solutions, the fall was even more striking. Thus, in the naphthalene solutions of runs 1 and 2 of Table 4, only 20 minutes' total irradiation was enough to reduce intensity of triplet absorption to 14% and 11%, respectively, of the initial value.

* The present demonstration of a low triplet concentration does not conflict with the high concentrations (up to 89%) of total solute found by Lewis, Calvin, and Kasha (*J. Chem. Phys.*, 1949, **17**, 804) in their work on the paramagnetism of acid fluorescein ($\tau_p^0 = 2{\cdot}8$ sec.) in boric acid glass, for in their measurements a much greater irradiation intensity was used.

This kind of effect should be accompanied by a diminution in the intensity of phosphorescence, and this was indeed noticed by Nauman (Thesis, University of California, Berkeley, 1947) in respect of toluene and numerous other substances. The original intensity of phosphorescence was restored by melting and refreezing the solutions. The light-filtering effect of the slowly-formed photodecomposition products could well cause our observed diminution in triplet absorption, and hence account for the failure of McClure's inferential method of arriving at extinction coefficients. This explanation is not unique, however, and has some difficulties. Thus, with anthracene, for which McClure again obtained low extinction coefficients, the triplet–triplet absorption did *not* fall off demonstrably. Again, it is not clear why this absorption should fall to a limiting value distinctly in excess of zero. A final decision concerning this effect must await further study.

Experimental

(5.1) *Absorption Cell.*—In order to transmit short-wave-length radiation, the cell containing the sample, and the Dewar vessel in which it stands, must be largely constructed of silica; for the same reason, liquid nitrogen is the only convenient refrigerant. The cell containing the solution was a silica tube terminating in a flat silica disc. At the top of the tube was a ground cone, over which fitted a Pyrex socket with a short length of tube attached. Across the top of the socket was stretched between steel flanges a Neoprene diaphragm with a circular hole in the centre; metal and glass were bonded with Araldite resin. Through the hole in the diaphragm there penetrated an evacuated Pyrex tube with flat silica end-plates, the lower plate providing a flat top surface for the solution. The lower part of this tube was externally platinized to prevent stray light from being scattered into the system from the surface of the quietly boiling refrigerant. The evacuated tube could slide through the diaphragm, so allowing the cell length to be varied. The cell stood in an unsilvered silica Dewar vessel, having flat inner and outer bottom surfaces. The contact between the bottom of the cell and the floor of the Dewar vessel was never precise enough to exclude liquid nitrogen, and without further precautions the light path would thus have been interfered with by streams of nitrogen bubbles. These were excluded by pushing the end of the cell through a hole in a small square of cloth, and later packing the cloth down firmly round the bottom of the cell. It was then almost always possible so to adjust the location and tilt of the cell so that no bubbles crossed the light path. The cloth packing served also to prevent ice crystals in the nitrogen from drifting under the cell. In use, hot air was directed against the lower surface of the Dewar flask, and ice-free liquid nitrogen was supplied every few minutes.

(5.2) *Irradiation of Rigid Solutions.*—As shown in Fig. 2 the cell was irradiated around the circumference. Excitation was provided either by up to three Osram type-MB/V 125-w medium-pressure mercury arcs (from which the glass envelopes had been removed), with reflectors, or by the spiral, low-pressure mercury–neon arc described by Ingold and Wilson (*J.*, 1936, 944) placed alongside the cell. The former lamps emit chiefly in the visible, and at 3346 and 3650 Å (these last lines being used for the excitation of most of the substances examined); the latter is an exceedingly intense source of the 2537 Å line, but its emission could not be very efficiently concentrated on the cell. The medium-pressure lamps were the more commonly used. Their infra-red emission being considerable, it was essential that they be shielded from the sample by a suitable heat filter, since neither nitrogen nor silica absorbs in the near infra-red. An annular silica filter cell was used, shown in section in Fig. 2; it was filled with distilled water.

The length of the cell actually irradiated was at most 10 cm.; the medium-pressure lamps being only 3 cm. long, this illumination was not uniform along the length of the cell. As far as possible the exciting lamps were screened to prevent stray light from entering the spectrophotometer; a small amount of such exciting light was found useful, however, the mercury lines thus detected being used for wave-length calibration.

(5.3) *Light-absorption Measurements.*—The source *S* (Fig. 2) was usually a 1000 c.p. " Pointolite " lamp. Light from *S* was collimated, passed downwards through the sample, and then reflected along the optic axis of a Cary Recording Spectrophotometer (Model 10). It was focused at the focus of the entrance lens of the spectrophotometer, *i.e.*, at the point normally occupied by the light sources in the conventional use of this instrument. The spectrophotometer was used on *single-beam* operation, recording intensity against wave-length. The intensity at a wave-length λ depended on the brightness of the lamp, the slit widths, and the

alignment of the optical system. A typical trace of the recorder pen deflection, $I_0(\lambda)$ against λ, for light passing through a rigid glass without irradiation is shown in Fig. 8; the curve has a flat maximum at about 5500 Å and falls off rapidly to the red and less rapidly toward the violet. Below 4050 Å gaseous emission bands become increasingly prominent and, near the glass cut-off at 3000 Å, they provide most of the intensity. With one single instrument setting a spectrum could be measured over about 500 Å; settings were then changed and a further stretch was measured until the whole spectrum was covered. The focused light beams gave pen deflections comparable to those obtained in normal Cary operation with the tungsten lamp. Typical slit widths are given in Table 5.

TABLE 5. *Typical working slit widths using* 1000 *c.p. light source.*

Wave-length (Å)	7600	7000	6000	5000	4000	3600	3200
Linear slit width (mm.)	0·27	0·075	0·016	0·014	0·027	0·054	0·20
Spectral slit width (Å)	97	23	3·4	1·8	1·7	2·4	6·0
Spectral slit width (cm.$^{-1}$) ...	168	47	9·4	6·8	11	19	59

For measurements below 3000 Å, and in some cases below 3500 Å, the positive crater of a carbon arc gave a continuous source of high brightness. Fluctuations were somewhat troublesome but qualitative observations were possible with it, and moderately strong T–T bonds would undoubtedly have been detected.

Measurements with fogged photographic plates of known spectral characteristics showed that the deflection of the recorder-pen was strictly proportional to the incident light intensity

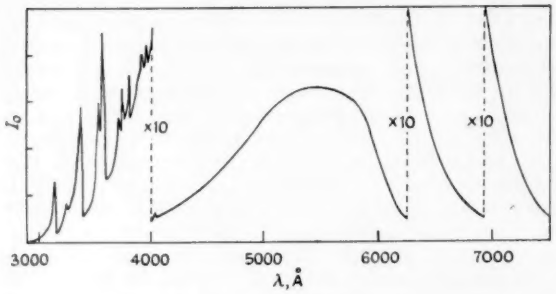


FIG. 8. Spectrum of Pointolite source, as measured by the Cary spectrophotometer.

at any wave-length. If, when the sample was irradiated, triplet–triplet absorption occurred, then the intensity at wave-length λ fell from $I_0(\lambda)$ to $I_t(\lambda)$, say, although this measured intensity would sometimes include a contribution $I_s(\lambda)$ due to luminescence of the solution and scattered exciting light. The apparent optical density (2.2) at wave-length λ was then

$$\rho_A(\lambda) = \log\{I_0(\lambda)/[I_t(\lambda) - I_s(\lambda)]\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The measurement of triplet–triplet absorption thus required three traces: $I_0(\lambda)$ obtained with the source S alone; $I_s(\lambda)$ obtained with the exciting lamps only, and $I_t(\lambda)$ obtained with both source and excitation. A typical set of three such curves is shown in Fig. 9. From these an optical density curve is obtained by applying eqn. (1) at sufficient points. The relation between the optical-density curve so obtained and T–T extinction coefficients is discussed in (2.3). One further source of possible error must be mentioned. The different relative triplet concentrations used in each region had to be determined from the ratios of the optical densities observed in regions where the spectra overlap: they were not, as in conventional spectrometric practice, known precisely. Errors thus introduced are naturally cumulative as one moves along a series of spectral regions.

(5.4) *Preparation of Rigid Solutions, and Purification of Materials.*—The solvent EPA consisted of ether, *iso*pentane, and ethanol (4 : 4 : 1 by vol.); the composition was altered from that introduced by Lewis and Kasha (*J. Amer. Chem. Soc.*, 1944, **66**, 2100) in order to reduce the tendency of this glass to shatter at the top of the frozen column, where the strain must be considerable even with careful freezing. The solvent PMh contained *iso*pentane and methyl*cyclo*hexane in the proportions 5 : 1; no trouble with cracking was experienced with this glass. In either case, however, the freezing of the solutions was always performed very carefully, over a period of at least 45 min., to produce a glass as free as possible from strain and lens effects (there is a contraction of over 20% on cooling these solvents to liquid nitrogen temperature).

The considerations which influence the choice of solvent are the necessity to avoid the photoreactions which may occur in EPA [cf. (3.2)], and the relative ease of handling; EPA is the more convenient, since no especial precautions are needed, when preparing the solutions, to avoid the ingress of atmospheric moisture. However, with PMh, unless such precautions are taken (see below), the rigid glass appears milky by reflected light, and yellow by transmitted light; this is probably due to short-wave-length light scattering by microscopic ice crystals

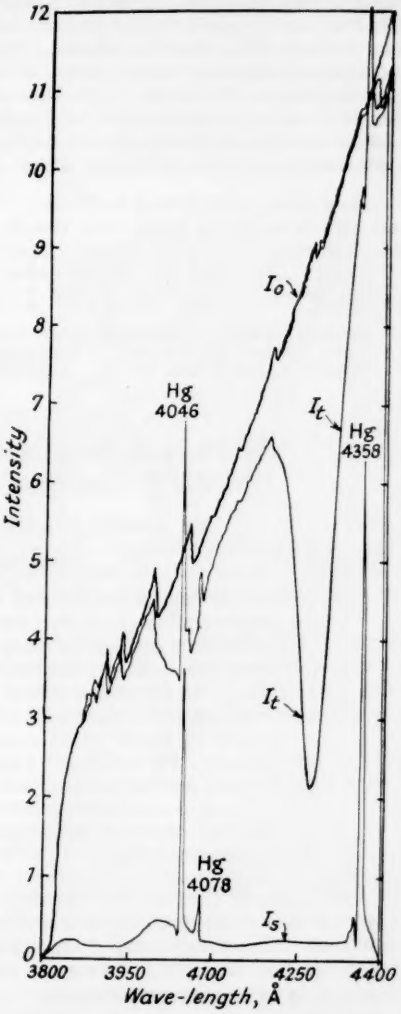


FIG. 9. Typical set of three curves, showing the triplet–triplet absorption bands of anthracene. The two upper traces each consist of two superimposed traces, measured in the order I_0, I_t, I_0 (repeat), I_t (repeat), and illustrate the satisfactory reproducibility obtainable under favourable conditions. The comparative unimportance of interference by scattered mercury lines and the intense anthracene fluorescence (trace I_s) is apparent. The record terminates at 3800 Å, owing to the ordinary absorption of the solute.

(Potts, *J. Chem. Phys.*, 1952, **20**, 809; Passerini and Ross, *J. Sci. Instr.*, 1953, **30**, 274). With EPA such scattering sets in rather sharply near 2800 Å (in 10-cm. path length), and for the most part this wave-length lay beyond the spectral range searched for T–T absorption.

To avoid this loss in transmission at short-wave-length, PMh solutions were made up entirely in an atmosphere of dry nitrogen, and were refluxed in the process to achieve some measure of degassing (Potts, *loc. cit.*). The solvents were premixed and kept over phosphoric oxide for 24 hr. before use; the solution, once prepared, was introduced into the assembled cell through a capilliary tube pushed down between the evacuated tube and the Neoprene diaphragm (Fig. 2). To avoid contamination by lubricating greases, the place of stopcocks in this apparatus was taken by Neoprene tubing provided with screw-clips.

Solvents. Ether and alcohol were purified by appropriate drying and distillation (cf. Sinsheimer, Scott, and Loofbourow, *J. Biol. Chem.*, 1950, **187**, 299); B.D.H. *iso*pentane and methyl*cyclo*hexane were purified by treatment with sulphuric acid, and subsequent passage through silica gel (cf. Potts, *loc. cit.*) or else through activated charcoal, previously heated under vacuum to remove the large water content.

Solutes. Benzene was a highly purified sample, prepared from "AnalaR" benzene by chemical pre-treatment, followed by repeated recrystallization; hexamethylbenzene, naphthalene, fluorene, diphenyl, diphenylamine, and acridine were reagent-grade samples purified by several recrystallizations from alcohol. Resublimed and chromatographed anthracene of high purity was provided by Dr. P. C. Hobbins. The four- and five-ring hydrocarbons were synthetic samples given us by Dr. E. M. F. Roe and chromatographed by Prof. R. Curti. Pyridine, quinoline, and *iso*quinoline were fractionally vacuum-distilled in an efficient column, and had refractive indices in agreement with the literature values. Small samples of the larger heterocyclics were given to us by Prof. A. Albert and were once recrystallized.

The authors are indebted to Dr. Roe, Prof. Albert, and Dr. Hobbins for gifts of chemicals, and wish especially to thank Prof. Renato Curti, of the University of Pavia, for carrying out the chromatographic purifications. They have benefited, too, from discussions with Prof. M. Kasha. This work was largely carried out during the tenure of an Australian National University Scholarship by one of them (I. G. R.).

WILLIAM RAMSAY & RALPH FORSTER LABORATORIES, UNIVERSITY COLLEGE, LONDON.
FLORIDA STATE UNIVERSITY, TALLAHASSEE.
(Present address of both authors: UNIVERSITY OF SYDNEY.) [*Received, November 19th*, 1953.]

The Thermal Decomposition of Guanidine Perchlorate. Part III. Catalysts and Time-lag before Ignition.*

By ABRAHAM GLASNER and ABRAHAM MAKOVKY.

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The kinetics of the thermal decomposition of guanidine perchlorate in the presence of catalysts were studied. The catalysts are divided according to their effects and known properties into three groups: (1) basic oxides, (2) redox catalysts, (3) catalysts for the synthesis (or decomposition) of ammonia. In the proposed reaction mechanism a definite role is assigned to the intermediary formation of perchloric acid.

Conditions under which guanidine perchlorate explodes or deflagrates are defined. The activation energies obtained from the rate of decomposition, and from the times of induction before the ignition of guanidine perchlorate and of ammonium perchlorate, average about 31·3 kcal./mole, indicating that the rates of these three processes are determined by the same fundamental reaction.

IN Part I (*J.*, 1953, 182) the behaviour of guanidine perchlorate on thermolysis and the mechanism of decomposition, and in Part II the kinetics of this decomposition have been described. The present paper reports measurements of the time lag (induction period) before ignition, and the influence of catalysts on the thermal decomposition of guanidine perchlorate at several temperatures.

EXPERIMENTAL

Guanidine perchlorate (m. p. 240°) was prepared as described in Part I. Ammonium perchlorate and potassium perchlorate were of Baker's Analysed C.P. grade. Dicyandiamide, guanidine chloride, and the various oxides used as catalysts were all analytical reagents.

The apparatus for kinetic measurements consisted of a Pyrex reaction vessel and reaction tube connected to a gasometer which contained saturated salt solution for levelling (Glasner and Weidenfeld, *J. Amer. Chem. Soc.*, 1952, **74**, 2464) in a manually-controlled electric furnace fitted with calibrated chromel–alumel thermocouples.

* Part II, *Bull. Res. Council, Israel*, 1953, 89.

For experiments with catalysts or other added materials, the ingredients were weighed separately and mixed in the reaction tube. Decompositions made in the same reaction tube gave closely reproducible curves, but on changing the reaction tubes different rates were obtained at the same temperature, even when the dimensions of the tubes were nearly the same. Therefore, series of runs to be compared with each other were always carried out in the same tube.

For the measurement of the time lag, the reaction vessel was replaced by a vertical Pyrex tube closed at the bottom into which a micro-test-tube was lowered on copper wire. When the system attained the desired constant temperature, the test tube was raised for a moment and a weighed sample of guanidine perchlorate (~70 mg.) dropped into it. The time lag was measured by a chronometer (to 0·01 min.) as the time from the moment the tube was returned to the furnace until a flash was seen, or a quick deflagration with a hissing noise was heard.

The same tube was used for a series of measurements, and it was thoroughly cleaned before each experiment. Values reported are the mean of at least three measurements, the maximum difference between two extreme readings at the same temperature being always less than 0·05 min.

Results

Time Lag.—The mean induction periods of ignition of guanidine perchlorate and ammonium perchlorate are recorded in the Table. The lags for ammonium perchlorate were larger than those of guanidine perchlorate at the same temperature but a mixture of 26·3% dicyandiamide and 73·7% ammonium perchlorate (having the overall composition of guanidine perchlorate) gave values similar to those for pure guanidine perchlorate.

Time lag before ignition.

Guanidine perchlorate :	Temp., °c	390	400	415	427	440
	10^2t, min.	256	166	93·6	79	51·7
Ammonium perchlorate :	Temp., °c	440	452	460	478	
	10^2t, min.	130	94	63	42	

Small additions of the oxides of iron(III), copper(II), cobalt(II), vanadium(V), and chromium(III) to guanidine perchlorate, ammonium perchlorate, or ammonium perchlorate–dicyandiamide mixtures greatly reduced the minimum temperature of ignition, in some cases to just above 300°.

As a rule, all oxides that cause an explosive reaction with guanidine perchlorate do the same with ammonium perchlorate though at a somewhat higher temperature. For example, mixtures of CuO, Ag_2O, Hg_2O, and MoO_3 with guanidine perchlorate exploded at 300°, 320°, 345°, and 345°, respectively, whilst mixtures of the same oxides with ammonium perchlorate exploded at 345° (CuO) and at 400° (MoO_3).

When the log of the induction period (Fig. 1) is plotted against the reciprocal of the absolute temperature the apparent energies of activation for guanidine perchlorate and for ammonium perchlorate are found to be 30·5 and 31·0 kcal./mole.

Kinetic Measurements.—The rates of evolution of gaseous products from guanidine perchlorate at four different temperatures between 345° and 380° have been measured. A plot of the percentage of gas evolved against time t, shows a slow acceleration of the reaction up to about 15% after which a constant rate of gas evolution is reached. Above 70% decomposition, a new increase in the reaction rate occurs accompanied by a rise in temperature so that the pyrolysis may end in a final deflagration followed by a small decrease in volume when the gases have cooled again to the constant temperature of the furnace. If powdered Pyrex glass (10%) is added to the guanidine perchlorate, the pyrolysis is more regular and the plot of the volume of gas evolved against reaction time is a straight line.

The rate constant k for the middle part of the thermal decomposition may be expressed by the equation $k = 2{\cdot}4 \times 10^{11}e^{-32400/RT}$ %/min. (see Fig. 2).

For comparison, equimolar mixtures of dicyandiamide (26·3 mg.) with ammonium perchlorate (73·7 mg.), and of guanidine chloride (59·7 mg.) with ammonium perchlorate (73·7 mg.), were decomposed at 355° and 365°. Points for both mixtures fall approximately on the same curve at corresponding temperatures (the times of slow reaction seem to be shortened somewhat in comparison with those for guanidine perchlorate, and there is also a slight increase in the slope of the main reaction curve). Mixtures of guanidine chloride (59·7 mg.) with potassium perchlorate (86·8 mg.) have a very slow rate of thermal decomposition.

The catalytic effect of some dry metal oxides was examined. They were mixed with the guanidine perchlorate in amounts approximately proportional to their formal weights (2—5% by wt). The reaction curves obtained at various temperatures are shown in Figs. 3(*a*, *b*, *c*).

FIG. 1. *Logarithm of the induction time,* t, *as a function of the reciprocal of absolute temperature.*

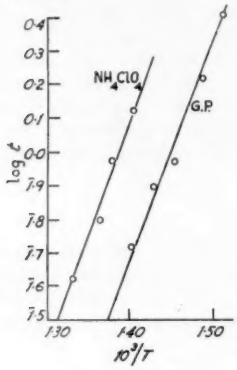

FIG. 2. *Logarithm of the rate constants* k *as a function of the reciprocal of absolute temperature.*

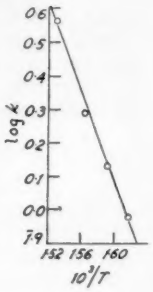

FIG. 3. *Decomposition* (%) *of guanidine perchlorate as a function of time in the presence of catalysts.*

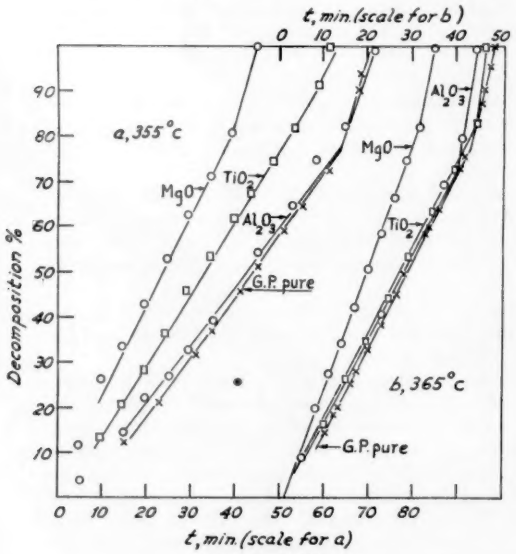

FIG. 3*a and* 3*b*.

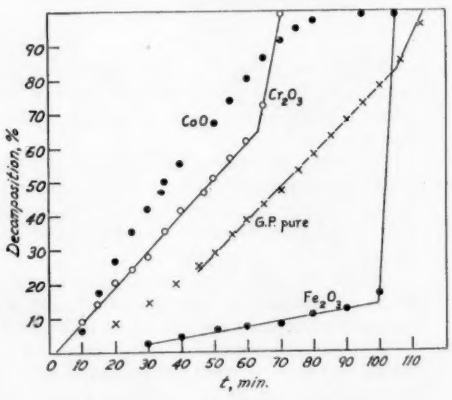

FIG. 3*c*.

CoO *and* Fe_2O_3 *at* 296°; *Guanidine perchlorate and* Cr_2O_3 *at* 345°.

The catalysts may be divided according to their effects into the following groups:

(1) Metal oxides with a constant valency, such as MgO and Al_2O_3, exert a small accelerating effect, but do not change the general character of the pyrolysis.

(2) Oxides of the transition metals, such as TiO_2, Cr_2O_3, and CoO, have a more pronounced catalytic effect and may cause an explosion or early deflagration at comparatively low temperatures.

(3) Some specific metal oxides (and metals), *e.g.*, V_2O_5, Fe_2O_3, (CuO), and platinum (in the form of a small foil), cause an explosion at any temperature above 300°. In this connection

the decomposition curves of guanidine perchlorate with Fe_2O_3 and with CoO at 296° (see Fig. 3*c*) are of a special interest.

Discussion

The reaction curves for the decomposition of guanidine perchlorate are composed of three nearly straight lines with increasing slopes. The main reaction covers from 15—20 to 75—85% of the decomposition and is of zero order and was shown to be catalysed by Pyrex glass, of which the reaction tubes consisted.

The following considerations give an insight into the nature of the reaction. The fact that pure guanidine perchlorate and its mixtures with equimolar amounts of ammonium perchlorate decompose at the same rate, indicates that ammonium perchlorate is produced from guanidine perchlorate in a primary reaction which, however, is not the determining step in the thermal decomposition of guanidine perchlorate. On the other hand, the very slow rate found for a guanidine chloride–potassium perchlorate mixture (which at the temperatures employed forms a homogeneous melt) excludes the possibility that the perchlorate ion is involved in this reaction. It is therefore suggested that free perchloric acid is the effective oxidising agent. The step determining the extent of the main reaction would then be the dissociation of ammonium perchlorate taking place on the walls of the reaction vessel: $NH_4ClO_4 \longrightarrow NH_3 + HClO_4$(3′) (following the numbering of the equations adopted in Part I). This is in agreement with the sequence of reactions proposed in Part I on the basis of the analysis of the products of the thermal decomposition of guanidine perchlorate:

$$CN_3H_5,HClO_4 \longrightarrow CN{\cdot}NH_2 + NH_3 + HClO_4 \quad . \; . \; . \; . \; . \; . \quad (3)$$

$$3CN{\cdot}NH_2 \longrightarrow C_3H_6N_6 \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (4)$$

$$C_3H_6N_6 \text{ and other condensates} + HClO_4 \longrightarrow \text{gaseous products} \quad . \; . \; . \quad (5)$$

The amendment suggested now implies that reaction (3) consists of two distinct steps, the second supplying the oxidising agent, perchloric acid. For the rate of oxidation, as measured by the volume (v) of permanent gases evolved, one can thus write in general terms:

$$dv/dt = k_5[\text{condensates}]^m[HClO_4]^n \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (6)$$

If a stationary concentration of the perchloric acid is assumed to exist during the main reaction stage, the change of perchloric acid concentration with time will be given by the equation

$$d[HClO_4]/dt = k - k_5[\text{condensates}]^m[HClO_4]^n = 0 \quad . \; . \; . \; . \; . \; . \; . \quad (7)$$

where k is the reaction constant of (3) or (3′).

By substitution of (7) into (6) k is obtained. Thus the decomposition of guanidine perchlorate is seen to be a simple function of the rate of production of perchloric acid, which is a constant determined by the area of contact between the walls of the reaction vessel and the ammonium perchlorate present.

The comparatively slow reaction at the beginning of a run is explained by the initial absence of ammonium perchlorate. Indeed, in mixtures initially containing ammonium perchlorate there is no induction period. The final deflagration may be ascribed to the amount of organic matter decreasing below a certain limit, whilst perchloric acid continues to be produced at the same constant rate.

For example, it has been shown in Part I that at lower temperatures a relatively large proportion of ammonia escapes oxidation so that the concentration of free perchloric acid in the reaction mixtures will be greater at low than at high temperatures, and the percentage of guanidine perchlorate decomposed before deflagration sets in is gradually lowered with decreasing temperature.

The above observation may help to elucidate the specific step of the postulated sequence of reactions influenced by a catalyst: A substance that will catalyse only reaction (5) (oxidation) will deter deflagration, whilst one that catalyses reaction (3) (formation of free perchloric acid) will shorten the main thermal decomposition and cause an early

deflagration. Many of the oxides used by us seem to catalyse both reactions (3) and (5) in varying measures, thus giving a variety of reaction curves.

1. *Basic oxides.* The perchlorates of these are known to hydrolyse at the temperature of the experiments into the oxides and free perchloric acid (Marvin and Woolaver, *Ind. Eng. Chem. Anal.*, **1945**, **17**, **474**); they may accelerate the evolution of ammonia because of their basicity, increasing thereby the rate of production of perchloric acid, and subsequently the rate of oxidation. A good example is magnesium oxide which accelerates the pyrolysis but does not change the general form of the curves. On the other hand, alumina, having a lower basicity, shows no appreciable effect on the decomposition.

2. *The oxides of transition metals.* These may act as basic oxides and also as agents for the transfer of oxygen. A comparison between the effects of chromium oxide and titanium oxide may illustrate this point. The former, combining the two properties mentioned, greatly accelerates the decomposition, and causes an early deflagration. On the other hand, titanium oxide accelerates only the rate of oxidation but does not enhance the formation of free perchloric acid so that deflagration occurs only at a later stage of decomposition.

3. *Catalysts of the type employed in the synthesis of ammonia.* These seem to form a special group with regard to their catalytic influence on the decomposition of guanidine perchlorate. This group is represented by Fe_2O_3, (CuO), V_2O_5, and platinum metal. They are all good catalysts for oxidation reactions, Fe_2O_3 and CuO having basic properties in addition. The catalytic effect of these substances is the most violent, being enhanced probably by the partial non-oxidative decomposition of ammonia caused by them.

Judged from its effectivity, cobalt oxide might be classified with the third group of catalysts; in fact it is but an extreme example of the catalysts of group 2, being more effective than chromium sesquioxide because of its higher basicity. This point is well brought out by comparing the decomposition curves of the mixtures of ferric oxide and cobalt oxide with guanidine perchlorate at 296°. At this low temperature cobalt oxide does not act any more as a hydrolytic agent, but its properties as an oxidation catalyst are very pronounced. Indeed, one of us (A. G., unpublished work) has shown that cobalt oxide catalyses the oxidation of organic salts (for example sodium formate) by potassium perchlorate at 200°.

Further evidence that the decomposition of ammonia is involved in the occurrence of explosions is obtained from the fact that all catalysts causing explosion of guanidine perchlorate show a similar effect in their mixtures with ammonium perchlorate, though at a somewhat higher temperature. Oxides which do not interfere with the decomposition of ammonia may cause a deflagration of guanidine perchlorate only after the elapse of a considerable period of induction. In the same way, the difference in the temperature of explosion of guanidine perchlorate and ammonium perchlorate observed with the pure substances (cf. the Table) may be due to the interaction between the organic substance and the perchloric acid. Some evidence to prove this suggestion has been obtained by the effective lowering of the explosion temperature of ammonium perchlorate to 390° by the addition of very small amounts of dicyandiamide or methyl methacrylate.

The activation energies obtained from the rate of decomposition of guanidine perchlorate, and the respective time lags before explosion for guanidine perchlorate and for ammonium perchlorate, are all close to about 31·3 kcal. This tends to confirm the view that the mechanism of the decomposition of these two substances is governed by the rate of the dissociation of ammonium perchlorate.

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The Hebrew University, Jerusalem, Israel.
Scientific Department, Israeli Ministry of Defence, Tel-Aviv.

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Fatty Acids. Part II. The Nature of the Oxygenated Acid present in* Vernonia anthelmintica *(Willd.) Seed Oil.*

By F. D. Gunstone.

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Vernolic acid, reported to be 11-hydroxyoctadec-9-enoic acid † (Vidyarthi, *Patna Univ. J.*, 1945, **1**, 51) is now shown to be 12 : 13-epoxyoctadec-9-enoic acid. The approximate composition of *V. anthelmintica* seed oil has been determined.

In Part I,* *Strophanthus sarmentosus* seed oil was shown to contain 9-hydroxyoctadec-12-enoic acid isomeric with the more familiar ricinoleic (12-hydroxyoctadec-9-enoic) acid of castor oil. 9-Hydroxyoctadec-12-enoic acid is now known to occur in other species of the *Strophanthus* genus (Gunstone, *J. Sci. Food Agric.*, 1953, **4**, 129). The isolation of this acid casts some doubt on the structure of similar hydroxy-acids, present in other fats, which have been described as ricinoleic acid merely on the basis of iodine value, equivalent, and acetyl value, and accordingly a number of these fats are being reinvestigated. This paper deals with *Vernonia anthelmintica* seed oil which has been reported to contain 11-hydroxyoctadec-9-enoic acid, another isomer of ricinoleic acid (Vidyarthi, *Patna Univ. J.*, 1945, **1**, 51).

It is further hoped that this study of naturally occurring oxygenated acids may contribute to the solution of the problem of the biogenesis of seed oils, since the hydroxy-acids present in seed fats may be the immediate precursors of the widely occurring unsaturated acids (oleic, linoleic, linolenic), which certain species or genera are unable, wholly or partly, to dehydrate, or alternatively may be examples of structures, not normally produced in plant systems, which, once formed, cannot be further metabolised owing to lack of suitable enzymes.

Vernonia anthelmintica (Willd.), syn. *Serratula anthelmintica* (Roxb.) and *Conyza anthelmintica* (Linn.), also known as the purple flea-bane and belonging to the family *Compositae*, is reported to be a tall robust leafy annual met with throughout India. Parts of the plant are said to have anthelmintic properties (Caius and Mhaskur, *Indian J. Med. Res.*, 1923, **11**, 353; Chopra, Ghosh, and Mukerji, *ibid.*, 1934, **22**, 183; Majumdar, *Indian J. Pharm.*, 1943, **5**, 61) and to be of value in the treatment of leucoderma (Ghosh, *Pharm. J.*, 1928, **121**, 54).

Chemical investigation of this seed oil has been reported by Kesava-Menon (*J. Soc. Chem. Ind.*, 1910, 1431), Vidyarthi and Mallya (*J. Indian Chem. Soc.*, 1939, **16**, 479), Majumdar (*loc. cit.*), and Vidyarthi (*loc. cit.*). These authors have drawn attention to the high acetyl value and optical rotation of this oil and have reported the presence of myristic, palmitic, stearic, oleic, linoleic, and vernolic acids among the component acids. The latter was considered to be 11-hydroxyoctadec-9-enoic acid.

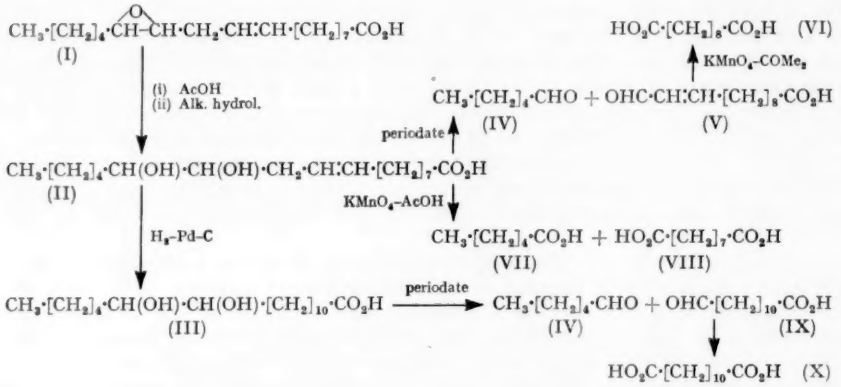
The Oxygenated Acid.—V. anthelmintica seeds were obtained from India (see p. 1616). The small green-brown bullet-shaped seeds yielded a dark green oil (26—27%) when extracted with light petroleum. Preliminary experiments showed that the oil contained an epoxy-acid; thus methanolic hydrogen chloride converted the acids into a product of low equivalent weight owing to the formation of a chloro-hydroxy-ester, whilst methanol containing concentrated sulphuric acid gave the hydroxy-methoxy-ester with a high equivalent weight (cf. Nicolet and Poulter, *J. Amer. Chem. Soc.*, 1930, **52**, 1186; Atherton and Hilditch, *J.*, 1943, 204; Swern, Findley, Billen, and Scanlan, *Analyt. Chem.*, 1947, **19**, 414; King, *Nature*, 1949, **164**, 706, *J.*, 1951, 1980). Quantitative determination of the epoxy-group (King, *loc. cit.*) showed that this was present in high proportions.

Because of the reactivity of the epoxy-compound it was converted into the corresponding dihydroxy-acid by treatment with acetic acid before the usual alkaline hydrolysis. A concentrate of the dihydroxyoctadecenoic acid was then easily prepared by partition of the

* Part I, *J.*, 1952, 1274.

† Geneva numbering, $CO_2H = 1$.

mixed acids between light petroleum and aqueous methanol. This readily gave a pure specimen of dihydroxyoctadecenoic acid which is almost certainly the *cis*-isomer and, after isomerisation of the concentrate, the higher-melting *trans*-isomer was also isolated. Hydrogenation of the mixed acids obtained on hydrolysis of the epoxide gave dihydroxystearic acid. Both the *cis*-unsaturated and the saturated acid showed a small lævorotation. Reinger (*Ber. deut. Pharm. Ges.*, 1922, **32**, 124) has described 12 : 13-dihydroxyoctadec-9-enoic acid as a syrupy liquid, whilst McKay and Bader (*J. Org. Chem.*, 1948, **13**, 75) have described the *cis*- and the *trans*-isomer of 9 : 10-dihydroxyoctadec-12-enoic acid as a liquid and a solid (m. p. 97°) respectively. The two racemic forms of 12 : 13-dihydroxyoctadecanoic acid are well known.



Dihydroxystearic acid (III), treated with periodate (King's procedure, *J.*, 1938, 1826; 1942, 387; cf. Huber, *J. Amer. Chem. Soc.*, 1951, **73**, 2730), gave a volatile aldehyde (not isolated) and a solid aldehydo-acid ($C_{12}H_{22}O_3$) which must be 11-formylundecanoic acid (IX) since oxidation gave dodecanedioic acid (X). The acid (IX) has not previously been described, though its methyl ester is known (Tomecko and Adams, *J. Amer. Chem. Soc.*, 1927, **49**, 529; Lycan and Adams, *ibid.*, 1929, **51**, 627). An attempt to prepare the semicarbazone of (IX) gave a product containing only a little nitrogen, possibly a derivative of a polymer.

The concentrate of the dihydroxyoctadecenoic acid (II), when similarly oxidised, gave a volatile aldehyde, the 2 : 4-dinitrophenylhydrazone of which gave correct analyses and had the same m. p. as that of *n*-hexanal (IV). The other product was an unsaturated aldehydo-acid ($C_{12}H_{20}O_3$) which readily gave a deep orange 2 : 4-dinitrophenylhydrazone. This was formulated as 11-formylundec-10-enoic acid (V) since oxidation gave sebacic acid (VI). The ultra-violet absorption spectrum showed that the double bond was conjugated with the carbonyl or the carboxyl group, and the former was preferred because of the deep colour of the 2 : 4-dinitrophenylhydrazone, and the lack of absorption in the original dihydroxyoctadecenoic acid.

Another portion of the concentrate of the dihydroxyoctadecenoic acid (II) was oxidised with potassium permanganate in acetic acid (Armstrong and Hilditch, *J. Soc. Chem. Ind.*, 1925, **44**, 43T), a method which is known to indicate satsifactorily the position of double bonds (cf. Begemann, Keppler, and Boekenoogen, *Rec. Trav. chim.*, 1950, **69**, 439). This gave *n*-hexanoic acid (VII) and azelaic acid (VIII) in good yield.

These results indicate that the dihydroxy-acid is 12 : 13-dihydroxyoctadec-9-enoic acid. Only one result is at variance with this conclusion, the appearance of 11-formylundec-10-enoic acid (V) as a product of periodate oxidation. Movement of double bonds into conjugation occurs frequently, though more generally in alkaline conditions. The author is unaware of any previous report of a double-bond shift under the very mild conditions of periodate oxidation, but this is what seems to have happened.

The original acid must clearly have been 12 : 13-epoxyoctadec-9-enoic acid, a result somewhat different from the earlier conclusions of Vidyarthi (*loc. cit.*) which were based on the isolation of azelaic acid and " a hydroxy-acid (m. p. 70°, equivalent 172) considered to be hydroxypelargonic " as products of the oxidation of methyl vernolate. Considerable modification of the epoxy-acid must have occurred during the preparation of methyl vernolate, and it is very unlikely that 2-hydroxynonanoic acid would result from oxidation; further degradation would surely occur.

Discussion of Quantitative Data.—12 : 13-*Epoxyoctadec-9-enoic acid.* Determination of the epoxide by King's method (*loc. cit.*) showed the oil to contain 67·1% of epoxyoctadecenoic glyceride.

The mixed acids obtained after acid and alkaline hydrolysis were esterified and the saponification equivalent was determined before and after acetylation. From these values it is possible to calculate the acetyl value (209·1) (cf. Riley, *Analyst*, 1951, **76**, 40; Gupta, Hilditch, and Riley, *J. Sci. Food Agric.*, 1951, **2**, 245). This is equivalent to 72·6% (wt.) of dihydroxyoctadecanoic acid. Before comparing this value with that for epoxyglyceride, allowance must be made for (*a*) a change in molecular weight, and (*b*) the removal of much of the unsaponifiable material (7·0%) before the second determination. Expressed as a molecular percentage of the acids (excluding unsaponifiable) these values correspond to 70·1% of epoxy-acid and 70·7% of dihydroxy-acid. It is proposed to use the mean of these values. The absence of dihydroxystearic acid before hydrogenation has been demonstrated.

The dihydroxyoctadecenoic acid does not show any ultra-violet light absorption after alkali isomerisation (Hilditch, Morton, and Riley, *Analyst*, 1945, **70**, 67). Its iodine value is higher than the calculated value, indicating some interaction between the reagents and the hydroxyl groups (cf. Part I; also McKay and Bader, *loc. cit.*, who report that both *cis*- and *trans*-9 : 10-dihydroxyoctadec-12-enoic acid have the correct iodine value).

Other acids present. Although the component acids present in this seed oil have not been quantitatively determined in the usual manner involving distillation, an approximate analysis has been made in the following way. As already described a concentrate of the dihydroxy-acid was prepared by partition. The light petroleum extracts (18%), containing only minor amounts of the dihydroxy-acid, were esterified, distilled and analysed in the usual way. This does not account for the non-hydroxy-acids in the methanol extracts but, on the assumption that these are similar in composition to those remaining in the petroleum, the composition of the acids (excluding unsaponifiable matter) is given in Table 1 (given to 0·5% because of their approximate nature; palmitic, stearic, and linoleic acids were identified in the usual way).

TABLE 1. *Component acids (% wt.) of* V. anthelmintica *seed oil.*

	Saturated					Unsaturated		
	C_{12}	C_{14}	C_{16}	C_{18}	C_{20}	Oleic	Linoleic	" Vernolic "
Present work	—	0·5	3·5	1·5	—	6·0	16·5	72·0
Vidyarthi	Trace	7·5	7·3	6·0	Trace	5·8	9·8	63·6

Conclusion.—This investigation has shown clearly that vernolic acid is 12 : 13-epoxyoctadec-9-enoic acid. Now that the structure is known it is suggested that the trivial name be dropped and be replaced by the systematic name or by 12 : 13-epoxyoleic acid. This is the first time that an epoxy-acid has been shown to occur in natural fats, though mono- and di-hydroxy- and keto-acids are known.

Reports of the occurrence of oxygenated acids have to be accepted with reserve for there are several examples where the reported claim was later disproved. Oxygenated acids of the C_{18} series which may be accepted as confirmed are set out in Table 2.

Much more information is obviously required before the structure of these acids can be used as evidence in any theory of the biogenesis of unsaturated acids in seed oils, but it is apparent that with one exception the monohydroxy-acids carry their hydroxyl group on C_9, C_{12}, or C_{18}. If these acids are built up from a three-carbon unit (cf. Hilditch, *Nature*, 1951, **167**, 298) then C_9, C_{12}, and C_{18} along with C_3, C_6, and C_{15} will represent the same carbon

atom of that unit. 12 : 13-Epoxyoleic acid may be related to 12-hydroxyoleic acid (ricinoleic) since stereospecific bio-hydrogenation could convert the former into the latter (cf.

TABLE 2. *Occurrence of oxygenated acids in natural fats.*

Acid	Formula	Species	Family
Ricinoleic	$CH_3\cdot[CH_2]_5\cdot CH(OH)\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$	Several *Ricinus* spp.	Euphorbiaceae [a]
9-Hydroxyoctadec-12-enoic	$CH_3\cdot[CH_2]_4\cdot CH{:}CH\cdot[CH_2]_2\cdot CH(OH)\cdot[CH_2]_7\cdot CO_2H$	Several *Strophanthus* spp.	Apocynaceae [b]
18-Hydroxyelæostearic	$HO\cdot[CH_2]_4\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$	*Mallotus philippinensis*	Euphorbiaceae [c]
12 : 13-Epoxyoleic acid	$CH_3\cdot[CH_2]_4\cdot CH(O)CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2H$	*Vernonia anthelmintica*	Compositae [d]
Unsaturated derivative of 8-hydroxystearic	$CH_3\cdot[CH_2]_9\cdot CH(OH)\cdot[CH_2]_6\cdot CO_2H$	*Onguekoa Gore*	Olacaceae [e]
9 : 10-Dihydroxystearic	$CH_3\cdot[CH_2]_7\cdot CH(OH)\cdot CH(OH)\cdot[CH_2]_7\cdot CO_2H$	Several *Ricinus* spp.	Euphorbiaceae

[a] Hilditch, "The Chemical Composition of Natural Fats," Chapman and Hall, London, 2nd Edn., p. 170. [b] Gunstone, *locc. cit.* [c] Aggarwal *et al.*, *J. Sci. Ind. Res., India*, 1948, **7**, *B*, 136; 1951, **10**, *B*, 76; 1952, **11**, *B*, 463; Calderwood and Gunstone, *Chem. and Ind.*, 1953, 436. [d] Present work. [e] Riley, *J.*, 1951, 1346. [f] Eibner and Münzing, *Chem. Umschau*, 1925, **32**, 159.

Mack and Bickford, *J. Org. Chem.*, 1953, **18**, 686, who have recently reported the stereospecific catalytic reduction of 9 : 10-epoxystearic acid).

EXPERIMENTAL

V. anthelmintica *Seed Oil.*—The seeds (286 g.; 100 = 0·45 g.) were coarsely ground and extracted (Soxhlet) with light petroleum (b. p. 40—60°). Removal of the solvent left a viscous green liquid (71·4 g.) which solidified at 0°. Regrinding and re-extraction gave a little more oil (5·4 g.; total, 26·9% of the seeds). The oil had sap. equiv. 322·9, I val. 107·6, unsap. 7·9 (S.P.A. Committee, *Analyst*, 1933, **58**, 203), free acid 26·4% (as epoxyoleic), and epoxide 67·1% (as epoxyglyceride).

Attempted Esterification of the Mixed Acids.—The oil (54·0 g.) was hydrolysed, by boiling alcoholic potassium hydroxide, to the mixed acids (52·1 g.; sap. equiv. 314·1, I val., 111·1). When treated with methanol (40 ml.) containing hydrogen chloride at room temp. for 24 hr. then at the b. p. for 45 min., the acids (8·1 g.) gave esters (8·5 g.) of low equivalent weight (255·6), but when refluxed with methanol (50 ml.) and concentrated sulphuric acid (0·5 ml.) the acids (8·6 g.) gave a product (9·3 g.) of high equivalent weight (350·7).

Conversion of Epoxy-glycerides into Dihydroxy-acids.—*V. anthelmintica* seed oil (98·4 g.) was boiled with acetic acid (700 ml.) for 7 hr. After removal of some solvent (500 ml.) the residue was diluted with water and extracted. The product was then hydrolysed by boiling alcoholic potassium hydroxide, and unsaponifiable material (6·81 g., 7·0%) removed by the S.P.A. method (*loc. cit.*; the quantities of solvents and reagent were increased proportionately). Acidification and extraction gave the required acids (91·1 g.; epoxide, nil) in which the material present in the oil as epoxy-glyceride had been converted into the corresponding dihydroxy-acid.

Determination of Dihydroxyoleic Acid.—The foregoing acids (21·8 g.) were esterified (22·1 g.) with methanolic hydrogen chloride at room temperature overnight and some of the esters (11·1 g.) acetylated by boiling with acetic anhydride (35 ml.) for 2 hr. and for a further hour after the addition of water (25 ml.), the acetylated esters (12·5 g.) being isolated by ether-extraction. Quadruplicate determination of the equivalent weight of both ester and acetylated ester gave the following results:

Ester	319·7	320·4	319·4	320·2	(Mean) 319·9
Acetylated ester	157·3	157·2	157·0	157·2	(Mean) 157·2

The acetyl value is given by the equation Ac val. $= (B - A)/(1 - 0{\cdot}00075A)$, where A and B are the sap. values of the ester and the acetylated ester respectively. (This relation is quoted by Riley, *loc. cit.*, for ricinoleic acid but can be shown to hold for a dihydroxy-acid.) These results give an acetyl value of 209·1 and indicate that the esters contain 72·6% (wt.) of methyl dihydroxyoctadecadienoate.

Another sample (4·89 g.) of acids obtained after hydrolysis of epoxides, which did not crystallise from ethyl acetate at 0°, was hydrogenated in presence of palladium–charcoal. Hydrogen, equiv. to 371 ml. at N.T.P., was quickly absorbed; this corresponds to an iodine val. of 86·0, compared with 100·8 measured with Wijs reagent in the usual way. The product (4·87 g.), crystallised from ethyl acetate (50 ml.) at 0°, gave 3·63 g. of insoluble material (74·5% of the dihydroxy-acid without a solubility correction; cf. Riley, *loc. cit.*).

Examination of the Non-hydroxylic Acids.—Light petroleum (b. p. 40—60°; 1 l.), methanol (800 ml.), and water (200 ml.) were equilibrated by shaking. The acids (58·8 g.) obtained after hydrolysis of epoxides were shaken with the petroleum phase (500 ml.) and the aqueous methanol phase (200 ml.), the methanol extract being re-extracted with light petroleum (2 × 100 ml.). Further methanol extracts (3 × 100 ml.) were made, each being re-extracted as above. In this way 7 solutions were obtained, and the solvent was removed from each. Fraction 7 was considered to be a concentrate of the dihydroxy-acid and was used in experiments described below.

	Light petroleum			Aq. methanol			
No.	1	2	3	4	5	6	7
Vol. (ml.)	500	100	100	100	100	100	100
Wt. (g.)	8·62	0·76	1·05	0·14	0·37	1·94	45·19

Fractions 1—3 (10·43 g.) were combined, esterified with methanol and concentrated sulphuric acid, and the resulting esters (10·39 g., iodine val. 113·2) were distilled through an electrically heated and packed column (Towers 117) with the following results:

Fraction no.	1	2	3 *	4	Res †
Wt. (g.)	1·78	1·80	2·28	2·54	1·86
Iodine val.	37·7	137·1	144·6	133·0	99·7
Sap. equiv.	271·7	290·3	292·6	293·4	327·5

* The acids from this fraction after isomerisation (180°/60 mm.) had $E^{1\%}_{1\,cm.}$ 636·4 at 234 mμ; for the unisomerised acids the value was only 5·2.

† 1·4803 g. of this residue contained 0·0984 g. of unsaponifiable material.

The esters thus have the following composition (as acids, % wt.): myristic 2·5, palmitic 11·9, stearic 4·4, oleic 20·4, linoleic 53·3, dihydroxyoleic acid 6·3, and unsaponifiable material 1·2%. Dihydroxyoleic acid has already been shown to account for 70·4% (mol.) of the acids and if it is now assumed that all of the non-hydroxy-acids (29·6% mol.) are present in the same proportion as in the distilled sample, the composition of the hydrolysed acids and hence of the original component acids can be computed to be as in Table 1.

Palmitic (m. p. 62—63°) and stearic (m. p. 68—70·5°) acids were obtained from fractions 1 and 4 respectively, and 9 : 10 : 12 : 13-tetrabromostearic acid (m. p. and mixed m. p. 112—113·5°) was prepared by bromination of the acids from fraction 3. Attempts to identify oleic acid in fraction 4 as dihydroxystearic acid were unsuccessful.

12 : 13-*Dihydroxystearic Acid* (III).—Crystallisation of the hydrogenation product described above from chloroform or ethyl acetate yields 12 : 13-*dihydroxystearic acid*, m. p. 95—96° [mixed m. p. with 9 : 10-dihydroxystearic acid (91—93°) was 83—86°] (Found: C, 68·3; H, 11·0. $C_{18}H_{36}O_4$ requires C, 68·3; H, 11·5%). The following were prepared by standard methods: *methyl ester*, m. p. 67·5—69° (Found: C, 69·1; H, 11·4. $C_{19}H_{38}O_4$ requires C, 69·1; H, 11·6%); *ethyl ester*, m. p. 61—63° (Found: C, 69·6; H, 11·5. $C_{20}H_{40}O_4$ requires C, 69·7; H, 11·7%); p-*bromophenacyl ester*, m. p. 102—106° (Found: C, 60·8; H, 8·0; Br, 15·9. $C_{26}H_{41}O_5Br$ requires C, 60·8; H, 8·0; Br, 15·6%).

Periodate Oxidation of 12 : 13-*Dihydroxystearic Acid.*—A solution of potassium periodate (0·6 g.) in N-sulphuric acid (30 ml.) was added to the dihydroxy-acid (0·8 g.) in ethanol (40 ml.) at 40° and the mixture kept at this temperature for 15 min., water (100 ml.) was then added, and the solution extracted with ether (5 × 70 ml.). The solvent was removed and the product steam-distilled. The residual solution, cooled to 0°, deposited a solid which was filtered off, dried, and extracted with light petroleum (b. p. 40—60°; 40 ml.). The extract, on cooling, gave 11-*formylundecanoic* (IX) which, after repeated crystallisation from the same solvent, melted at 60—62° (Found: C, 67·1; H, 10·5. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·4%).

Some of the crude compound treated with semicarbazide hydrochloride and sodium acetate gave a crystalline product, m. p. 103·5—107° (Found: C, 66·3; H, 10·1; N, 3·2%).

Another portion of the formyl compound suspended in dilute sulphuric acid was treated with excess of potassium permanganate solution on a steam-bath for 40 min. The solution, when

decolourised (sulphur dioxide) and cooled to 0°, gave crystals of dodecanedioic acid (X), m. p. 124—126° after crystallisation from ethyl acetate; this was raised to 125—127° when mixed with an authentic specimen (lit., 128°).

12 : 13-*Dihydroxyoctadec*-cis-9-*enoic Acid* (II).—A pure sample of 12 : 13-*dihydroxyoctadec*-cis-9-*enoic* acid was readily obtained from the concentrate of this acid (fraction 7 of the aqueous methanol–light petroleum partition) by crystallisation from a mixture (1 : 1) of ether and light petroleum (b. p. 40—60°), m. p. 53—54° (Found : I val., 95·8; C, 68·7; H, 10·6%. $C_{18}H_{34}O_4$ requires I val., 80·8; C, 68·8; H, 10·9%); its p-*bromophenacyl ester* had m. p. 72—74° (Found : C, 61·0; H, 7·8; Br, 15·4. $C_{26}H_{39}O_5Br$ requires C, 61·1; H, 7·7; Br, 15·6%).

When heated at 180° for 1 hr. with a solution (7½%) of potassium hydroxide in ethylene glycol, 12 : 13-dihydroxyoleic acid shows practically no absorption at 234 mμ ($E^{1\%}_{1\,cm.}$ 3·8).

12 : 13-*Dihydroxyoctadec*-trans-9-*enoic Acid*.—The concentrate of dihydroxy-acid (6·5 g.) was suspended in 50% nitric acid (2·6 ml.) at 60° during addition of sodium nitrite solution (0·2 g. in 1·3 ml. of water) and then kept at 55—65° for 10 min. The product was extracted and after prolonged storage in ether–light petroleum (b. p. 40—60°) a small quantity of the *trans*-acid was obtained, m. p. after several crystallisations 67·5—69·5° (Found : C, 68·8; H, 10·8%); its p-*bromophenacyl ester* had m. p. 84·5—86° (Found : C, 61·3; H, 7·6; Br, 15·8%).

Periodate Oxidation of 12 : 13-*Dihydroxyoctadec*-cis-9-*enoic Acid*.—This acid (2·0 g.) was oxidised by the method described above. Extraction of the steam-distillate afforded hexanal [2 : 4-dinitrophenylhydrazone, m. p. 102·5—104° (lit., 104°) (Found : C, 51·7; H, 5·9; N, 19·8. Calc. for $C_{12}H_{16}O_4N_4$: C, 51·4; H, 5·8; N, 20·0%)]. The non-volatile fraction gave 11-*formylundec*-10-*enoic acid* (V), m. p. 65—66°, absorption max. at 224 mμ (log ε 4·02 in EtOH) (Found : C, 68·0; H, 9·5. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%). Its 2 : 4-*dinitrophenylhydrazone*, m. p. 81·5—83·0° (Found : C, 55·3; H, 6·3; N, 14·2. $C_{18}H_{24}O_6N_4$ requires C, 55·1; H, 6·2; N, 14·3%), was obtained from ethanol as deep orange crystals.

Oxidation of (V) by potassium permanganate in aqueous acid or acetone gave sebacic acid, m. p. and mixed m. p. 129·5—131·5°.

Permanganate Oxidation of 12 : 13-*Dihydroxyoctadec*-cis-9-*enoic Acid*.—To the concentrate of dihydroxyoleic acid (3·76 g.), dissolved in acetic acid which had been purified by treatment with potassium permanganate, finely powdered permanganate (10 g.) was added portionwise, the temperature being kept below 50°. When all the reagent had been added and the temperature began to fall the mixture was kept at 40—50° for 3 hr. The solvent was then removed under reduced pressure and the product, suspended in dilute sulphuric acid, decolourised with sulphur dioxide. The resulting mono- and di-basic acids were separated by steam-distillation and extracted from the volatile and the non-volatile portions respectively.

Distillation of the volatile acids (1·89 g.) under reduced pressure gave a small fore-run (63 mg.), probably acetic acid, and a remainder which distilled as a single fraction (531 mg.). This was converted to its *p*-bromophenacyl ester, m. p. 70—71° (undepressed when mixed with the ester of hexanoic acid) (Found : C, 53·5; H, 5·5; Br, 25·6. Calc. for $C_{14}H_{17}O_3Br$: C, 53·7; H, 5·5; Br, 25·5%).

The non-volatile product (2·27 g.) was extracted with boiling water (170 ml. in four portions) and filtered from insoluble oil. The filtrate, reduced to small volume, gave azelaic acid (1·00 g.) when cooled to 0°. After crystallisation from ethyl acetate this had m. p. and mixed m. p. 103—106°.

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The Calculation of Bond Orders, Resonance Energies, and Orbital Energies by a Simple Perturbation Method.

By M. J. S. Dewar and R. Pettit.

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By using the perimeter model as a basis and by considering the introduction of cross links as a perturbation, an estimate of the resonance energies, orbital energies, and bond orders of polycyclic aromatic hydrocarbons can be obtained in a much simpler manner than by the usual L.C.A.O. procedure. A linear correspondence exists for the values of the resonance energies predicted by the two methods; there is also a close agreement for the orbital-energy estimates. Some differences do occur between the two methods in the calculated bond orders and predicted bond lengths: a comparison with the experimental values for naphthalene and anthracene shows the L.C.A.O. method and the simpler new method to be about equal in the accuracy of their predictions.

The molecular orbital method has been successfully used to account for the physical and chemical behaviour of conjugated organic molecules. Its basic conception is that the electrons of a conjugated system occupy molecular orbitals covering the entire extent of the conjugation, and in the L.C.A.O. M.O. approach the wave functions of these orbitals can be written as linear combinations of the wave functions of the various atomic orbitals involved in the conjugated system. Thus the electronic energy levels in the molecule can be determined, as well as resonance energies and bond orders. Unfortunately, in many cases, and in common with alternative methods, the straightforward L.C.A.O. M.O. treatment loses much of its appeal by virtue of the tedious calculations involved. However, it is found that, as in other branches of quantum mechanics, considerable simplification can often be introduced by use of perturbation methods. Largely because of the inclusion of perturbation methods into the M.O. theory and of the resulting simplifications a general theory has been devised which can now serve as a basis for the theoretical study of many organic compounds (Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341, 3345, 3350, 3353, 3355, 3357, and references therein; Dewar and Pettit, following paper).

It is also encouraging that in the process of simplifying the usual L.C.A.O. treatment by the inclusion of perturbation methods the validity of the results is not necessarily decreased. This fact is amply demonstrated in the calculations of the frequency of the first absorption bands of complex aromatic hydrocarbons where the predicted values given by perturbation methods are much more easily obtained and, indeed, are in far better agreement with experiment, than those obtained by the straightforward M.O. method (Dewar, *J.*, 1952, 3532).

The present paper describes how the inclusion of perturbation methods assists in the M.O. evaluation of orbital energies, resonance energies, and bond orders of polycyclic aromatic hydrocarbons; the usual M.O. calculations of these quantities are extremely tedious in such compounds, especially those having more than three fused rings and having no symmetry properties. In principle the present treatment considers a polycyclic aromatic hydrocarbon as formed by the introduction of certain cross-links into a completely conjugated cyclic polyene, *e.g.*, naphthalene is considered as formed from *cyclo*decapentaene by means of a link between $C_{(1)}$ and $C_{(6)}$. The orbital energies and bond orders of a cyclic polyene can be written down on sight and it only remains to find what effects the perturbations, *i.e.*, the introduction of the various internal cross-links, have on these values. Perimeter models have already been used by Platt (*J. Chem. Phys.*, 1949, **17**, 484) in connection with the spectra of aromatic hydrocarbons.

Method

Orbital Energies and Resonance Energies.—The electrons of a cyclic polyene occupy orbitals which are all doubly-degenerate, except for the lowest, which is non-degenerate. The co-

efficients of the wave functions of the atomic orbitals in each molecular orbital have the values $\sin n\pi x/k$ and $\cos n\pi x/k$. The wave functions of the molecular orbitals are given by:

$$\left.\begin{aligned} \Psi\,(\sin) &= \sum_x A \sin\,(n\pi x/k)\,.\,\psi_x \\ \text{and} \qquad \Psi\,(\cos) &= \sum_x A \cos\,(n\pi x/k)\,.\,\psi_x \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where ψ_x is the $2p$ A.O. of atom number x.

The energy of each of these molecular orbitals is given by

$$E = -\,2\beta \cos 2n\pi/k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Where n is the quantum number of the orbital, k is half the total number of atoms, and A is a normalising factor having a value of $1/\sqrt{k}$ when $n \neq 0$ and $1/\sqrt{2k}$ when $n = 0$.

It will be seen that the numbering of the atoms in the polyene is purely arbitrary and to simplify the calculations it is desirable to introduce a phase factor ε such that the atomic orbital coefficients are given by the expressions:

$$A \sin\,[(n\pi x/k) + \varepsilon] \text{ and } A \cos\,[(n\pi x/k) + \varepsilon$$

No generality is lost because of this inclusion.

Now consider the formation of a bond between two non-adjacent atoms r, s of the polyene as being the perturbation. The basic zero-order wave functions for the first-order perturbation for a doubly degenerate level are then given by:

$$\begin{aligned} \Phi &= C_1\Psi\,(\sin) + C_2\Psi\,(\cos) \\ &= C_1 \sum_{x=1}^{n} A \sin\,[(n\pi x/k) + \varepsilon] + C_2 \sum_{x=1}^{n} A \cos\,[(n\pi x/k) + \varepsilon] \quad . \quad . \quad . \quad (3) \end{aligned}$$

The first-order perturbation energies are given by the standard secular equation

$$\begin{vmatrix} (H^1_{11} - E) & H^1_{12} \\ H^1_{12} & (H^1_{22} - E) \end{vmatrix} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

When the non-diagonal terms of the determinant are made to vanish the roots of the secular equation (4) become simply H^1_{11} and H^1_{22}.

The simplest way to solve equation (4), and simultaneously to determine the phase angle ε is to choose ε in such a way that the off-diagonal elements, H^1_{12}, in the determinant vanish. The roots of the secular equation then become H^1_{11} and H^1_{22}, and the coefficients of the atomic orbitals in the perturbed molecular orbitals become:

$$A \sin\,[(n\pi x/k) + \varepsilon] \text{ and } A \cos\,[n\pi x/k) + \varepsilon]$$

[since if H^1_{12} vanishes, either C_1 or C_2 in equation (3) vanishes]. Equating H^1_{12} to zero and considering the perturbation term, P, of the Hamiltonian to be the introduction of a cross-link between atoms r and s, we have:

$$H^1_{12} \equiv \int \Psi\,(\sin)\, P\Psi\,(\cos)\, d\tau = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

i.e.

$$\int \sum_{x=1}^{n} A \sin\,[(n\pi x/k) + \varepsilon] \sum_{x^1=1}^{n} A \cos\,[(n\pi x^1/k) + \varepsilon]\psi_x\,.\,P\psi_{x^1}\,d\tau = 0 \quad . \quad . \quad (6)$$

Now

$$\begin{aligned} \int \psi_x P\,.\,\psi_{x^1} d\tau &= -\,\beta \text{ when } x = r,\ x^1 = s \\ &\qquad\quad x^1 = r,\ x = s \\ &= 0 \text{ otherwise} \end{aligned} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Therefore, from (6), we have:

$$\sum_{\varepsilon}\{A \sin\,[(n\pi r/k) + \varepsilon] A \cos\,[(n\pi s/k) + \varepsilon] + A \sin\,[(n\pi s/k) + \varepsilon] \cos\,[n\pi r/k + \varepsilon]\} = 0\,. \quad (8)$$

where the summation is taken over all the cross-links formed in the molecule.

Now, from (8) we see that

$$\sum_{\varepsilon} \sin\,\{[n\pi(r + s)/k + 2\varepsilon]\} = 0$$

i.e.,

$$\sum_{\varepsilon} \sin\,[n\pi(r + s)/k] \cos 2\varepsilon + \sum_{\varepsilon} \cos\,[(n\pi(r + s)/k]\,.\,\sin 2\varepsilon = 0$$

Therefore,

$$\tan 2\varepsilon = -\,\frac{\sum_{\varepsilon} \sin\,[n\pi(r + s)/k]}{\sum \cos\,[n\pi(r + s)/k]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Equation (9) allows a determination of the phase factor and thereby allows simple expressions for the perturbation energies. In practice it is found that the phase factor need be calculated only for molecules having no plane of symmetry; in the other cases it can be made equal to zero by adopting the correct numbering, and this in turn can be found by inspection since the plane of symmetry must be a nodal plane for one member of each pair of degenerate eigenfunctions. The perturbation energies are then given by the equations:

$$E^1(\sin) = H^1_{11} = \int \Psi(\sin) \,.\, P \,.\, \Psi(\sin) \,.\, d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

and

$$E^1(\cos) = H^1_{22} = \int \Psi(\cos) \,.\, P \,.\, \Psi(\cos) \,.\, d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

From (10):

$$E^1 = \int \sum_{x=1}^{n} \sum_{x^1=1}^{n} A^2 \,.\, \sin(n\pi x/k) \,.\, \sin(n\pi x^1/k) \,.\, \psi_{(x)} \,.\, P \,.\, \psi_{(x^1)} \,.\, d\tau$$

where the phase factor has been embodied in the values x and x^1. When the values given in equations (7) are substituted for the integral equation (10) becomes:

$$\begin{aligned} E^1(\sin) &= -A^2\beta\{[\sin(n\pi r/k) \,.\, \sin(n\pi s/k)] + [\sin(n\pi s/k) \,.\, \sin(n\pi r/k)]\} \\ &= -A^2\beta\{\cos[n\pi(r-s)/k] - \cos[n\pi(r+s)/k]\} \quad . \quad . \quad . \quad . \quad . \quad (12) \end{aligned}$$

Similarly equation (11) simplifies to

$$E^1(\cos) = -A^2\beta\{\cos[n\pi(r-s)/k] + \cos[n\pi(r+s)/k]\} \quad . \quad . \quad . \quad (13)$$

When more than one cross-link is being formed the values are given by

$$E^1 \sin(\cos) = -\sum_{\text{cross links}} A^2\beta \{\cos[n\pi(r-s)/k] \,(\mp)\, \cos[n\pi(r+s)/k] \quad . \quad . \quad (14)$$

since first-order perturbations are additive.

Equations (14) now allow the determination of the change in energy of the orbitals of the cyclic polyene when cross-links are found to give the polycyclic compound.

The Figure illustrates how the method is used in the determination of the energy levels of naphthalene. The parent cyclic polyene is shown on the left; the cross-link is to be introduced

Energy levels of naphthalene, overlap being neglected.

Energy levels of polyene		Energy levels of naphthalene: Perturbation method	Energy levels of naphthalene: L.C.A.O. method
	− 0·618		
sin		− 0·618	− 0·618
cos		− 1·018	− 1·000
	− 1·618		
sin		− 1·218	− 1·304
cos		− 1·618	− 1·618
	− 2·00		
cos		− 2·200	− 2·301

between atoms 5 and 10, and the numbering of the ring is such as to allow the phase factor to vanish. The orbital energies (overlap being neglected) of the polyene are given in the first column and their new values, after the introduction of the cross-link, are shown in the second column. The third column gives the energy levels calculated by the usual L.C.A.O. procedure.

Similar calculations have been performed on sixteen polycyclic aromatic hydrocarbons, with the results given in Table 1, together with the corresponding values calculated by the usual L.C.A.O. method. Also given are the resonance energies and the four lowest electronic transition energies involved in light adsorption, together with a comparison of these values (both readily obtained from a knowledge of the orbital energies) with those obtained by the L.C.A.O. method.

Bond Orders.—By considering a polycyclic hydrocarbon as formed from a completely conjugated cyclic polyene by the introduction of cross-links, it is also possible to obtain a value of the bond orders of the polycyclic hydrocarbons in a simple manner. We make use of an expression, first introduced by Coulson and Longuet-Higgins (*Proc. Roy. Soc.*, **1947**, *A*, **191**, 39) and applicable to conjugated systems, termed the bond-bond polarizability. This value is defined * by:

$$\pi mn,\, tu = \frac{\partial p_{mn}}{\partial \beta_{tu}} = -2 \sum_r \sum_s \frac{(a_{mr}a_{ns} + a_{ms}a_{nr})(a_{tr}a_{us} + a_{ts}a_{ur})}{(\varepsilon_r - \varepsilon_j)} \quad . \quad . \quad . \quad (15)$$

* The negative sign in equation (15) arises because we have retained the original convention for the signs of energies.

TABLE 1. *Resonance energies, transition energies, and occupied molecular orbital energies of polycyclic hydrocarbons.*

Except for the resonance energies, where it has been neglected, a value of 0·25 has been taken for the overlap integral. The values are all in terms of γ, the appropriate unit when overlap is included. The L.C.A.O. values have been taken from data given by Pullman and Pullman, "Les Theories Electroniques de la Chimie Organique," Masson, Paris, 1952.

	Resonance energy		Electronic transitions		Orbital energies	
Compound	Perturbation method	L.C.A.O.	Perturbation method	L.C.A.O.	Perturbation method	L.C.A.O.
Naphthalene	**3·344**	**3·683**	1·266	1·266	0·535	0·535
			1·542	1·531	0·811	0·800
			1·902	1·869	0·934	0·983
			2·178	2·133	1·155	1·152
					1·419	1·461
Anthracene	4·622	5·314	0·847	0·837	0·379	0·375
			1·202	1·262	0·734	0·800
			1·539	1·709	0·794	0·800
			1·894	2·133	1·004	1·045
					1·075	1·045
					1·292	1·333
					1·455	1·506
Phenanthrene	4·618	5·448	1·314	1·239	0·552	0·526
			1·406	1·358	0·644	0·645
			1·501	1·478	0·804	0·889
			1·593	1·597	1·016	0·984
					1·018	1·100
					1·279	1·311
					1·455	1·514
Naphthacene	5·843	6·932	0·596	0·594	0·276	0·275
			0·892	0·970	0·572	0·651
			1·077	1·240	0·776	0·800
			1·373	1·616	0·863	0·919
					1·000	0·978
					1·035	1·073
					1·226	1·231
					1·361	1·417
					1·474	1·526
3 : 4-Benzophenanthrene	5·842	7·187	1·085	1·159	0·470	0·497
			1·230	1·230	0·615	0·568
			1·359	1·290	0·800	0·800
			1·504	1·361	0·800	0·877
					0·972	1·045
					1·064	1·045
					1·134	1·227
					1·339	1·392
					1·474	1·541
Triphenylene	5·904	7·275	1·233	1·409	0·524	0·584
			1·233	1·409	0·524	0·584
			1·233	1·409	0·690	0·721
			1·233	1·409	0·934	0·973
					0·934	0·973
					1·091	1·008
					1·252	1·320
					1·252	1·320
					1·474	1·551
Chrysene	5·840	7·190	1·027	1·058	0·449	0·460
			1·211	1·259	0·633	0·661
			1·375	1·448	0·672	0·718
			1·559	1·649	0·905	0·933
					0·923	0·973
					1·045	1·112
					1·193	1·193
					1·353	1·405
					1·474	1·538

TABLE 1. *(Continued.)*

Compound	Resonance energy		Electronic transition		Orbital energies	
	Perturbation method	L.C.A.O.	Perturbation method	L.C.A.O.	Perturbation method	L.C.A.O.
1 : 2-Benzanthracene	5·840	7·101	1·027	0·916	0·449	0·406
			1·211	1·117	0·633	0·607
			1·375	1·277	0·672	0·800
			1·559	1·477	0·905	0·903
					0·923	0·994
					1·045	1·084
					1·193	1·220
					1·353	1·409
					1·474	1·533
Pentacene	7·068	8·544	0·433	0·441	0·205	0·208
			0·676	0·768	0·448	0·535
			0·782	0·939	0·732	0·800
			1·025	1·266	0·763	0·800
					0·936	0·935
					0·942	0·983
					1·053	1·089
					1·154	1·152
					1·311	1·333
					1·409	1·461
					1·486	1·537
1 : 2-3 : 4-Dibenzanthracene ...	7·124	8·942	0·989	1·014	0·434	0·444
			1·088	1·176	0·533	0·606
			1·158	1·312	0·570	0·660
			1·257	1·475	0·769	0·859
					1·000	0·924
					1·065	0·991
					1·073	1·026
					1·073	1·204
					1·205	1·320
					1·350	1·428
					1·486	1·561
1 : 2-7 : 8-Dibenzanthracene ...	7·068	8·879	1·167	0·999	0·500	0·438
			1·179	1·096	0·512	0·535
			1·188	1·169	0·670	0·717
			1·200	1·266	0·755	0·800
					0·860	0·953
					0·997	0·983
					1·042	1·097
					1·069	1·152
					1·261	1·307
					1·389	1·461
					1·486	1·547
Picene	7·072	8·943	1·074	1·020	0·466	0·446
			1·154	1·155	0·546	0·581
			1·217	1·266	0·607	0·708
			1·297	1·401	0·814	0·800
					0·814	0·924
					0·970	1·018
					1·061	1·109
					1·089	1·123
					1·283	1·305
					1·394	1·459
					1·486	1·552
Pentaphene	7·072	8·763	1·074	0·885	0·466	0·394
			1·154	0·952	0·546	0·461
			1·217	0·993	0·607	0·800
			1·297	1·060	0·814	0·800
					0·814	0·944
					0·970	0·975
					1·061	1·093
					1·089	1·141
					1·283	1·333
					1·394	1·454
					1·486	1·544

TABLE 1. (*Continued.*)

Compound	Resonance energy: Perturbation method	Resonance energy: L.C.A.O.	Electronic transitions: Perturbation method	Electronic transitions: L.C.A.O.	Orbital energies: Perturbation method	Orbital energies: L.C.A.O.
1 : 2-5 : 6-Dibenzanthracene ...	7·072	8·880	1·074	1·016	0·466	0·443
			1·154	1·157	0·546	0·584
			1·216	1·269	0·607	0·657
			1·297	1·410	0·814	0·844
					0·814	0·913
					0·970	1·045
					1·061	1·045
					1·089	1·173
					1·283	1·301
					1·394	1·463
					1·486	1·547
Azulene	2·954	3·364	0·973	0·968	0·428	0·426
			1·266	1·268	0·721	0·726
			1·556	1·566	0·956	1·013
			1·849	1·866	1·171	1·169
					1·419	1·465
Pentalene	2·156	2·456	—	—	0·444	0·421
					0·745	0·800
					1·045	1·045
					1·440	1·478

where ∂p_{mn} is the change in bond order of the bond mn following a change in the resonance integral $\partial\beta_{tu}$ between atoms t and u; a_{mr}, a_{ns}, etc., are the coefficients of the atomic orbitals of atoms m, n, etc., in the rth and sth molecular orbitals respectively; and r and s refer in turn to the bonding and antibonding orbitals and have energy values of ε_r and ε_s respectively.

In the case of cyclic polyenes, where the energy levels are doubly degenerate, equation (15) can be shown to be also valid if the correct zero-order molecular orbitals given in the previous section are used as a basis in its derivation. It follows then that the change in bond order of the bond between atoms m and n in a cyclic polyene, caused by the introduction of a cross link between atoms t and u, is given by :

$$\partial p_{mn} = -2\beta \sum_r \sum_s \frac{(a_{mr}a_{ns} + a_{ms}a_{nr})(a_{tr}a_{us} + a_{ur}a_{ts})}{\varepsilon_r - \varepsilon_s} \quad . \quad . \quad . \quad . \quad (16)$$

This expression can be applied in the present calculations by using the values for the coefficient given in equation (1). Since each level is degenerate, we have

$$a_{mr} = \cos\,[(m\pi r/k) + \varepsilon]\,; \quad a^1_{mr} = \sin\,[(m\pi r/k) + \varepsilon]$$

these being the coefficients in the two distinct molecular orbitals ψm (cos) and ψm (sin) of common energy E_m.

If the alternate atoms of the cyclic polyene are starred, then, by using the fact that the coefficients of the atomic orbitals of starred atoms in the bonding molecular orbitals of alternate hydrocarbons are equal in magnitude and sign to the same coefficients in the corresponding antibonding orbitals whereas for unstarred atoms the two coefficients are of equal magnitude but differ in sign, equation (16) can be readily simplified to the form :

$$\partial p_{mn} = \frac{1}{k^2(1 - \cos s\pi/k)} \cdot \sum_{s \neq k} \left[\cos\frac{s\pi(m-u)}{k} + \cos\frac{s\pi(n-t)}{k} + \cos\frac{s\pi(m-t)}{k} + \cos\frac{s\pi(n-u)}{k}\right]$$

$$+ \frac{1}{k^2\left(\cos\dfrac{r\pi}{k} - \cos\dfrac{s\pi}{k}\right)} \sum_{r \neq 0} \sum_{s \neq k} \left[\cos\frac{r\pi(m-t)}{k} \cdot \cos\frac{s\pi(n-u)}{k} + \cos\frac{r\pi(m-u)}{k}\cos\frac{s\pi(n-t)}{k}\right.$$

$$\left. + \cos\frac{r\pi(n-t)}{k} \cdot \cos\frac{s\pi(m-u)}{k} + \cos\frac{r\pi(n-u)}{k} \cdot \cos\frac{s\pi(m-t)}{k}\right] \quad . \quad . \quad (17)$$

The first square bracket of this expression results from the combinations $r \neq 0$, $s = k$, and $r = 0$, $s \neq k$; and the second from $r \neq 0$, $s \neq k$; the value of the perturbation for the com-

bination $r = 0$, $s = k$ vanishes. As before, if more than one cross-link is formed the perturbations are additive.

The bond orders of polycyclic hydrocarbons are then found by adding the perturbation values given by equation (17) to the bond order of any bond in the unperturbed cyclic polyene; the bonds of the unperturbed polyene all have the same bond order which is given by :

$$p_{mn} = 2\sum_r A^2 \cos(\pi r/k) \text{ where } \left.\begin{array}{l} A^2 = 1/2k \text{ for } r = 0 \\ = 1/k \text{ for } r \neq 0 \end{array}\right\} \quad . \quad . \quad . \quad . \quad (18)$$

By this method the bond orders of naphthalene, anthracene, phenanthrene, 1 : 2-benzanthracene, and azulene have been estimated, with results given in Table 2 together with those

TABLE 2.

Compound	Bond	Bond order: Perturbation method	Bond order: L.C.A.O. method	Predicted bond length: Perturbation method	Predicted bond length: L.C.A.O. method	Obs. length
Naphthalene	*A*	0·732	0·725	1·38	1·38	1·36
	B	0·584	0·555	1·41	1·41	1·42
	C	0·638	0·603	1·40	1·40	1·395
	D	0·574	0·518	1·41	1·42	1·395
Anthracene	*A*	0·761	0·738	1·37	1·38	1·365
	B	0·565	0·535	1·41	1·42	1·42
	C	0·578	0·586	1·41	1·41	1·39
	D	0·557	0·485	1·41	1·43	1·44
	E	0·602	0·606	1·40	1·40	1·39
Phenanthrene	*A*	0·674	0·590	1·39	1·41	—
	B	0·663	0·702	1·39	1·38	—
	C	0·669	0·623	1·39	1·40	—
	D	0·669	0·705	1·39	1·38	—
	E	0·662	0·575	1·39	1·41	—
	F	0·532	0·506	1·42	1·42	—
	G	0·773	0·775	1·37	1·37	—
	H	0·490	0·461	1·43	1·43	—
	I	0·649	0·542	1·40	1·42	—
1 : 2-Benzanthracene ...	*A*	0·719	0·597	1·38	1·41	—
	B	0·635	0·695	1·40	1·38	—
	C	0·713	0·628	1·38	1·40	—
	D	0·637	0·700	1·40	1·38	—
	E	0·703	0·581	1·38	1·41	—
	F	0·492	0·493	1·43	1·43	—
	G	0·800	0·783	1·37	1·37	—
	H	0·503	0·494	1·42	1·43	—
	I	0·703	0·628	1·38	1·40	—
	J	0·572	0·590	1·41	1·41	—
	K	0·631	0·542	1·40	1·42	—
	L	0·709	0·732	1·38	1·38	—
	M	0·636	0·593	1·40	1·41	—
	N	0·706	0·731	1·38	1·38	—
	O	0·632	0·545	1·40	1·42	—
	P	0·560	0·584	1·41	1·41	—
	Q	0·725	0·646	1·38	1·395	—
	R	0·471	0·447	1·43	1·44	—
	S	0·680	0·478	1·39	1·43	—
	T	0·634	0·500	1·40	1·425	—
	U	0·622	0·495	1·40	1·43	—
Azulene	*A*	0·648	0·656	1·395	1·39	—
	B	0·648	0·596	1·395	1·41	—
	C	0·648	0·586	1·395	1·41	—
	D	0·648	0·664	1·395	1·39	—
	E	0·648	0·639	1·395	1·40	—
	F	0·420	0·401	1·44	1·45	—

found by the usual L.C.A.O. method. Also given are the bond lengths predicted by both methods (estimated from the Coulson bond-order–bond-length curve) and a comparison of these values with known experimental bond lengths.

Discussion

Although the resonance energies, calculated by each of the two methods show considerable discrepancies, yet if one set of values is plotted against the other it is seen that $A = 1{\cdot}35B - 0{\cdot}70$, where A and B are the resonance energies determined by the L.C.A.O. method and the perturbation method respectively. For the acene series of hydrocarbons the resonance energies are consistently lower than for the corresponding "branched" isomers and in these cases the relation $A = 1{\cdot}28B - 0{\cdot}56$ is better. The values given by these equations for the resonance energies are shown in Table 3: the very small percentage errors indicate that the simple perturbation method allows an accurate estimate of the L.C.A.O. resonance energies of alternant polycyclic hydrocarbons.

Table 3. *L.C.A.O. resonance energies predicted by the perturbation method, compared with the accurate values.*

Compound	Predicted	Found	Error (%)	Compound	Predicted	Found	Error (%)
Naphthalene	3·71	3·68	0·8	Pentacene	8·49	8·54	0·6
Anthracene	5·35	5·31	0·7	1 : 2-3 : 4-Dibenzanthracene	8·91	8·94	0·3
Phenanthrene	5·54	5·45	1·7	1 : 2-7 : 8-Dibenzanthracene	8·84	8·88	0·4
Naphthacene	6·92	6·93	0·2	Picene	8·84	8·94	1·1
3 : 4-Benzophenanthrene	7·18	7·19	0·1	Pentaphene	8·84	8·76	0·9
Triphenylene	7·27	7·28	0·1	1 : 2-5 : 6-Dibenzanthracene	8·84	8·88	0·4
Chrysene	7·18	7·19	0·1	Azulene	3·21	3·36	4·4
1 : 2-Benzanthracene	7·18	7·10	1·4	Pentalene	2·20	2·46	12

The correspondence of the values of orbital and transition energies given by the two methods is also sufficiently close to allow the simple method to have useful applications.

Discrepancies between the two methods are shown in the bond orders and the corresponding estimated bond length. The bond length D of naphthalene calculated by the perturbation method is in slightly the better agreement with experiment. For anthracene the perturbation method gives a better predicted value for bond A but worse values for B and D. The discrepancy for bond D may however not be as great as indicated, for there is some evidence that the experimental value is less than that given in Table 2 (Ahmed and Cruickshank, *Acta Cryst.*, 1952, **5**, 852). In the alternant hydrocarbons both methods commonly predict the bond possessing greatest chemical reactivity. It is interesting also that the introduction of a cross-link between atoms 1 and 5 in *cyclo*decapentaene has no effect on the bond orders; the bond orders of the external bonds in azulene are therefore all equal, and the same as those for *cyclo*decapentaene. It can be shown that this is a general result when a cross-link is introduced between two atoms of like parity, *i.e.*, both starred or unstarred, in a cyclic polyene. Another interesting feature of the perturbation method is that it predicts that all the external bonds of the outer rings in phenanthrene have the same lengths, as do those of benzene; there are also differences predicted by the two methods for 1 : 2-benzanthracene, and comparison with experimental values would be desirable.

So far the only compounds that have been treated by the above perturbation procedure are polycyclic aromatic hydrocarbons having no carbon atom common to more than two rings. It is hoped to extend the method to the more highly condensed systems and also to heterocyclic molecules.

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A Molecular-orbital Theory of Organic Chemistry. Part VII. The Additivity of Bond Energies in Unconjugated Systems.*

By M. J. S. Dewar and R. Pettit.

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The problem of additivity of bond energies in unconjugated compounds is discussed. The effect of interactions between localised bonds is calculated by perturbation theory, and it is found that the effect of such interactions vanishes to a first approximation. The second-order effects can to a large extent be absorbed into the empirical bond energies. In this way the additivity of bond energies in such compounds is explained without postulating localisation of electrons in specific bonds. Departures from additivity are satisfactorily interpreted and relations obtained which are shown to be in close agreement with experiment. It is deduced that the important interactions are those between adjacent bonds rather than 1 : 3 interactions of the type postulated in hyperconjugation. The present treatment avoids most of the assumptions made in the usual M.O. treatment and its conclusions should be correspondingly reliable.

In previous papers of this series (Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341, 3345, 3350, 3353, 3355, 3357) a general molecular-orbital treatment of organic chemistry was discussed and applied to the study of conjugated systems. Here unconjugated systems will be discussed in similar terms.

Unconjugated systems have been little investigated theoretically, and there has been a tendency to regard the bonds in such compounds as being formed by localised pairs of electrons with no significant interaction. This view seems to be supported by the fact that many properties of such compounds are additive functions of the bonds in them: for example, the heats of formation, dipole moments, and molar refractivities.

It has become apparent in recent years that this is too naïve. The electrons in a molecule are not localised in specific bonds but are dispersed to a greater or less extent over the whole molecule. It is true that the resonance theory appears to support bond localisation, but it does so only by virtue of its assumption that the ground states of molecules can be represented adequately in terms of unexcited structures. There is no theoretical justification for this, and it has been shown recently that the practical success of the resonance theory cannot be taken as evidence for the truth of its basic assumptions (Dewar and Longuet-Higgins, *Proc. Roy. Soc.*, 1952, *A*, **214**, 482). The apparent additivity of bond properties then raises an interesting theoretical problem which has not yet been convincingly solved.

Lennard-Jones and his collaborators (*Proc. Roy. Soc.*, 1949, *A*, **198** 1, 14; 1950, *A*, **202**, 155, 166, 323, 336) have examined the situation in unconjugated molecules in terms of the molecular-orbital theory. They found that the usual delocalised molecular orbitals in such a system can be replaced by an equivalent set of orbitals each essentially localised in a single bond. According to them an unconjugated molecule can be regarded in two different but equivalent ways: as a system in which the electrons occupy either delocalised molecular orbitals or localised "equivalent orbitals." The additivity of bond properties follows naturally, but the picture suffers from two defects. First, it does not explain in a simple qualitative manner why similar localised equivalent orbitals are not available in conjugated systems (see Hall, *Proc. Roy. Soc.*, 1950, *A*, **202**, 336, for the equivalent orbital treatment); and secondly, it does not account in any simple way for the second-order deviations from additivity of bond properties in unconjugated systems.

Not only are these second-order deviations appreciable but they also seem to follow definite rules. Platt (*J. Chem. Phys.*, 1947, **15**, 419), found empirically that the heats of formation of paraffins can be expressed with remarkable accuracy by a single set of bond

* Part VI, *J. Amer. Chem. Soc.*, 1952, **74**, 3357.

energies, together with a set of explicit corrections for structural features such as chain branching

Lennard-Jones and his collaborators have shown that an unconjugated molecule can be represented to a first approximation in terms of localised bonds. In considering such molecules to a higher approximation it is natural to regard the interactions between these localised bonds as small perturbations and to calculate their effect on the ideal localised structure by use of perturbation theory. This programme follows naturally from the earlier papers of this series where similar perturbation methods were used in discussions of the structures and properties of conjugated molecules.

We have taken as the unperturbed system one in which the bonds are represented by simple L.C.A.O. M.O. wave functions. Although these may differ from the equivalent orbitals of Lennard-Jones *et al.*, they serve equally well as a basis for the perturbational treatment; for it can be shown that the net effect of the mutual interaction of the occupied (bonding) orbitals vanishes (Brown and Dewar, *J.*, 1953, 2406). The only interactions that need to be considered are those between occupied (bonding) and unoccupied (antibonding) orbitals.

In this perturbation treatment overlap is necessarily neglected. It would of course be possible to include overlap in a variational treatment of the problem, using the localised molecular orbitals as a basis (cf. Dewar, *Proc. Camb. Phil. Soc.*, 1948, **45**, 648); but such a treatment would be tedious and unsuitable for the present purpose. Moreover, the inclusion of overlap in the simple L.C.A.O. treatment seems to make no appreciable difference, at any rate in the calculation of ground-state energies.

Brown (*J.*, 1953, 2615) considered the problem of localisation from a different but analogous point of view. He used the united-atom concept, expressing the molecular orbitals in a molecule as linear combinations of united-atom orbitals for the individual bonds. The appropriate linear combinations are found by a variation method with inclusion of overlap. This treatment is equivalent to that outlined above, except that only bonding orbitals are used as a basis. The omission of antibonding orbitals greatly simplifies the variational treatment.

If this correspondence between the two treatments is accepted, it is apparent that our approximations are more valid than Brown's. It is unjustifiable in theory to neglect the contribution of antibonding orbitals, since the set of functions used as a basis is then incomplete; and the practical consequences of such an omission are also rather striking. Consider, for example, the analogous treatment of a conjugated or aromatic hydrocarbon, derived by perturbation of one classical structure in which there are localised two-centre π-bonds. The M.O.'s for the molecule can be expressed as linear combinations of the π-M.O.'s of the individual π-bonds in the classical structure, the results being identical with those given by the usual L.C.A.O. M.O. treatment (cf. Dewar, *loc. cit.*, 1948). If, however, only the *bonding* M.O.'s are used as a basis, the total energy of the π-electrons turns out to be the same as in the classical structure; thus, in benzene, only three M.O.'s can be constructed from the bonding π-M.O.'s of a Kekulé structure, and the total energy of these is the same (-3β) as the total energy of the three localised bonding π-M.O.'s in the Kekulé structure. It is obvious therefore that if antibonding orbitals are neglected in this connection, the calculated resonance energies of all hydrocarbons are zero. If one regards an aromatic hydrocarbon as being derived from a classical structure by interaction between the localised π-bonds, it is evident that the interactions leading to resonance stabilisation are those between bonding and antibonding M.O.'s.

Resonance energy in our approximation is indeed a second-order effect, due to the mutual perturbation of bonding and antibonding orbitals. It is therefore impossible to place any confidence in a molecular-orbital treatment where the contribution of antibonding orbitals is neglected. On the other hand no case is known where the omission of overlap leads to serious practical errors in ground-state energies of molecules; and our neglect of this factor should not qualitatively effect our conclusions. The nature of our approximations will be considered in more detail below.

It is curious that the conclusions reached by Brown and by us agree closely in form, although the methods followed are basically dissimilar. However, our method predicts

accurate additivity of bond energies to a first approximation, departures from additivity being second-order effects, whereas Brown finds first-order departures from additivity. The experimental evidence seems to suggest that departures from additivity are second-order effects since they are so small.

Method and Results

The interaction between bonds is calculated by use of perturbation theory. In the unperturbed system the electrons occupy a set of localised non-interacting two-centre orbitals. The set of unperturbed orbitals also includes the corresponding antibonding orbitals. It is assumed that all bonds of a given type are similar in the unperturbed state. The energies of the bonding and antibonding M.O.'s between two atoms R, S are written respectively as ε^{+}_{RS}, ε^{-}_{RS}.

First-order Perturbations; Mutual Interactions of Bonding Orbitals.—First-order perturbations due to interaction of bonds arise only in the case of degeneracy (cf. Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341), *i.e.*, when the interacting bonds are similar. First-order perturbations therefore represent a special case of mutual interaction between filled or bonding orbitals. Now it can be shown (cf. Brown and Dewar, *J.*, 1953, 2406) that the total energy of a set of occupied orbitals is unaffected by interactions between them; although such interactions alter the individual energy levels they do not, therefore, alter the total energy of all the orbitals. It follows at once that the heat of formation of a molecule will be an additive function of the individual bond energies, to a first approximation, no matter what interactions arise between the bonds and no matter how large the resulting delocalisation of the electrons in the system. Brown (*loc. cit.*) reached the same conclusion.

Second-order Perturbations.—In a molecule there are commonly a number of bonds of each type (C–H, C–C, etc.). In considering the interactions of such bonds, the individual orbitals ($\phi^{\pm}_{RS}$) of each type should first be replaced by appropriate linear combinations (ψ_{RS}), found by the first-order perturbation theory for degenerate systems; and the second-order perturbations should be calculated by using these perturbed orbitals. This complicated procedure is totally unnecessary if the degenerate levels are all filled, as in the case here, and if only the total energy of the whole set of degenerate levels is required. In that case it can be shown (see Appendix A) that the same result is obtained if the second-order perturbations are calculated by using the set of unperturbed orbitals $\phi^{\pm}_{RS}$ and simply omitting terms with vanishing denominators. Also since mutual interactions between pairs of occupied orbitals cancel (see above), the second-order perturbations reduce to a series of terms of the form :

$$\delta E_{RS,\,TU} = \left[\int \phi^{+}_{RS} \cdot P_{RS,\,TU} \phi^{-}_{TU} \cdot d\tau\right]^2 / (\varepsilon^{+}_{RS} - \varepsilon^{-}_{TU}) \quad . \quad . \quad . \quad . \quad (1)$$

where $\delta E_{RS,\,TU}$ represents the second-order effect on the energy of the bonding orbital ϕ^{+}_{RS} due to interaction with the antibonding orbital ϕ^{-}_{TU} and $P_{RS,\,TU}$ is the term in the Hamiltonian representing this interaction.

In order to use this expansion some assumption must be made concerning the types of interaction between bonds. It will be assumed that the only interactions of importance are those between nearest-neighbour bonds, *i.e.*, bonds with a common atom such as the R–S and S–T bonds in RST. The total interaction energy in this case will be given by

$$\delta E_{RST} = \frac{\left[\int \phi^{+}_{RS} \cdot P_{RS,\,ST} \phi^{-}_{ST} \cdot d\tau\right]^2}{\varepsilon^{+}_{RS} - \varepsilon^{-}_{ST}} + \frac{\left[\int \phi^{+}_{ST} \cdot P_{ST,\,RS} \cdot \phi^{-}_{RS}\right]^2}{\varepsilon^{+}_{ST} - \varepsilon^{-}_{RS}}$$

Here δE_{RST}, the R–S–T interaction energy, will be a constant characteristic of the bonds concerned, if, as has been assumed, all bonds of a given type are similar in the unperturbed system and if the stereochemistry of the central atom S is also fixed.

These basic interaction energies can then be regarded as empirical parameters; and the total second-order perturbation energy can be expressed in terms of them simply by counting the number of structures of each type in the molecule.

Application to Paraffins.—In paraffins there are three basic interacting structures, C–C–C, C–C–H, and H–C–H. Denote the corresponding second-order perturbation energies by a, b, c, respectively. The total second-order perturbation energy can be expressed at once in terms of these parameters. This is done for the first five normal hydrocarbons in Table 1, where it is seen that, after ethane, the second-order perturbation increases by a uniform increment $(a + 4b + c)$ for each methylene group; this can be shown to hold generally. If it also held for methane–ethane the second-order perturbation energy for methane would be $(2b + 5c - a)$.

Suppose the ideal bond energies of localised C–C and C–H bonds to be respectively E°_{CC}, E°_{CH} and define empirical C–C and C–H bond energies E_{CC}, E_{CH} by the relations

$$\left.\begin{aligned} E_{CH} &= E^\circ_{CH} + \tfrac{1}{4}(2b + 5c - a) \\ E_{CC} &= E^\circ_{CC} + \tfrac{3}{2}(a + 2b - c) \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Then it is evident that use of these empirical bond energies in calculating heats of formation of normal paraffins other than methane will give values correct to a second approximation. For instance, the calculated heat of formation of propane will be given by

$$\begin{aligned} 2E_{CC} + 8E_{CH} &= 2E^\circ_{CC} + 8E^\circ_{CH} + 3(a + 2b - c) + 2(2b + 5c - a) \\ &= 2E^\circ_{CC} + 8E^\circ_{CH} + (a + 10b + 7c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4) \end{aligned}$$

and the final second-order correction agrees with that given in Table 1.

We can therefore choose empirical bond energies for the C–C and C–H bonds which will give calculated heats of formation for the *n*-paraffins correct to a second approximation. Since the interactions between bonds in paraffins are undoubtedly small, the third-order terms must

TABLE 1. *Total second-order perturbations in normal paraffins.*

Paraffin	Number of structures C–C–C	C–C–H	H–C–H	Total perturbation
CH_4	—	—	6	$6c$
C_2H_6	—	6	6	$6b + 6c$
C_3H_8	1	10	7	$a + 10b + 7c$
C_4H_{10}	2	14	8	$2a + 14b + 8c$
C_5H_{12}	3	18	9	$3a + 18b + 9c$

be very small indeed; the extraordinarily close approximation to additivity shown by heats of formation of *n*-paraffins is not therefore surprising.

The increment $(a + 4b + c)$ applies in all cases where a paraffin is extended by replacing a primary hydrogen atom by a methyl group. Replacing secondary or tertiary hydrogen gives different increments. The various values are

$$\left.\begin{aligned} R{\cdot}CH_3 &\longrightarrow R{\cdot}CH_2{\cdot}CH_3; \quad \delta E = a + 4b + c \\ R_2CH_2 &\longrightarrow R_2CH{\cdot}CH_3; \quad \delta E = 2a + 2b + 2c \\ R_3CH &\longrightarrow R_3C{\cdot}CH_3; \quad \delta E = 3a + 3c \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Now replacement of a secondary hydrogen atom gives a paraffin with a branch or, equivalently, with a tertiary $\gtrless$CH group; comparison with an isomer in which a primary hydrogen atom is replaced by a methyl group shows that the second-order perturbation energies differ by $(a - 2b + c)$. Likewise the difference in total second-order perturbation energies between a normal paraffin and an isomer with a double branch (*i.e.*, with a quaternary carbon atom) is seen to be $3(a - 2b + c)$, or three times the value for a single branch.

The heat of formation, ΔH, of an *iso*paraffin will then be given by

$$\begin{aligned} \Delta H = \Delta H_n + [&(\text{no. of tertiary carbon atoms}) \\ &+ 3(\text{no. of quarternary carbon atoms})](a - 2b + c) \quad . \quad . \quad (6) \end{aligned}$$

where ΔH_n is the heat of formation of the isomeric *n*-paraffin. This result agrees exactly with the relations found empirically by Platt (*loc. cit.*). It is difficult to predict theoretically the sign or magnitude of the term $(a - 2b + c)$; in practice it is found to be negative and about 1·3 kcal./mole.

If the bond energies in normal paraffins are additive the heats of formation should also be additive. The heat of formation, ΔH_n, of n-C_nH_{2n+2} should be given by

$$\Delta H_n = A + (n - 1)B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $A = 4E_{CH}$, $B = E_{CC} + 2E_{CH}$, and E_{CH}, E_{CC} are the C–H and C–C bond energies. Deviations from this relation are given in Table 2, with $A = -15{\cdot}31$ and $B = -4{\cdot}93$ kcal./mole, values used for the heats of formation at 25° being those given by Prosen and Rossini (*J. Res. Nat. Bur. Stand.*, 1945, **34**, 263). The deviations are seen to be very small, implying that bond energies are closely additive, except for methane. The abnormal stability of methane cannot be

explained in terms of the present treatment; indeed a positive deviation would have been expected. This anomaly may be due to the high symmetry of the methane molecule and the absence of bonds about which rotation can take place.

Deviations for singly branched and for *gem.*-branched paraffins are also given in Table 2. Both show systematic negative deviations, the mean deviation for *gem.*-branched paraffins being approximately three times that for singly branched paraffins, as is predicted.

TABLE 2. *Deviations from additivity in heats of formation of unstrained paraffins.*

Hydrocarbon	Deviation from additivity	Hydrocarbon	Deviation from additivity
n-Methane	−2·58	2 : 2-Dimethylpropane	−4·64
n-Ethane	0·00	2 : 2-Dimethylbutane	−4·37
n-Propane	+0·35	2 : 2-Dimethylpentane	−4·40
n-Butane	+0·29	3 : 3-Dimethylpentane	−3·28
n-Pentane	+0·03	2 : 2-Dimethylhexane	−3·89
n-Hexane	+0·00	3 : 3-Dimethylhexane	−2·79
n-Heptane	+0·00		
		Mean	−3·90
2-Methylpropane	−1·35		
2-Methylbutane	−1·89	2 : 4-Dimethylpentane	−3·41
2-Methylpentane	−1·70	2 : 4-Dimethylhexane	−2·62
3-Methylpentane	−1·08	2 : 5-Dimethylhexane	−3·39
2-Methylhexane	−1·71		
3-Methylhexane	−1·07	Mean	−3·14
2-Methylheptane	−1·68		
3-Methylheptane	−1·00		
4-Methylheptane	−0·58		
Mean	−1·34		

As Platt pointed out, the contributions of different branches in poly-branched paraffins are additive provided the branches are well separated; if the branches are close together, steric effects arise. This is seen particularly clearly in compounds with quaternary carbon atoms β to one another, *e.g.*, in poly*iso*butene (Brown and Barbaras, *J. Chem. Phys.*, 1946, **14**, 114) and in homomorphs of di-*tert.*-butylmethane (Brown, *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 1).

Data for doubly branched paraffins, with separated branches, given in Table 2, show that additivity holds quite accurately. The steric effects that arise when two or more branches are

TABLE 3. *Deviations from addivity in heats of formation of strained paraffins.*

Compound	Deviation from additivity Obs.	Calc.	Difference
2 : 3-Dimethylbutane	−2·53	−2·68	+0·15
2 : 3-Dimethylpentane	−2·73	−2·68	−0·05
2 : 2 : 3-Trimethylbutane	−4·07	−5·24	+1·17
2 : 3-Dimethylhexane	−1·31	−2·68	+1·37
3 : 4-Dimethylhexane	−1·09	−2·68	+1·59
3-Ethyl-2-methylpentane	−0·66	−2·68	+2·02
2 : 2 : 3-Trimethylpentane	−2·79	−5·24	+2·45
2 : 2 : 4-Trimethylpentane	−3·75	−5·24	+1·49
2 : 3 : 3-Trimethylpentane	−1·91	−5·24	+3·33
2 : 3 : 4-Trimethylpentane	−2·15	−4·02	+1·87
2 : 2 : 3 : 3-Tetramethylbutane	−3·17	−7·80	+4·63

TABLE 4. *Calculated total perturbation energies for olefins.*

Compound	δE	ΔE
$CH_2{=}CH_2$	$2c + 4e$	$a - 2b - 3c + 4e$
$CH_2{\cdot}CH{=}CH_2$	$4b + 4c + d + 3e$	$-2b - 2c + d + 3e$
$(CH_3)_2C{=}CH_2$	$a + 6b + 7c + 2d + 2e$	$-4b + 2d + 2e$
$CH_3{\cdot}CH{=}CH{\cdot}CH_3$	$8b + 6c + 2d + 2e$	$-a - 2b - c + 2d + 2e$
$(CH_3)_2C{=}CH{\cdot}CH_3$	$a + 10b + 9c + 3d + e$	$-a - 4b + c + 3d + e$
$(CH_3)_2C{=}C(CH_3)_2$	$2a + 12b + 12c + 4d$	$-a - 6b + 3c + 4d$

adjacent are illustrated in Table 3; the second column shows the observed deviations from additivity, and the third the deviations calculated on the assumption that the effects of branches are additive with values of −1·34 and −3·90 kcal./mole for single and *gem.*-branches respectively. The differences, shown in the last column, indicate the importance and magnitude of steric strain effects. Note that strain is significant only when the branches are large, or when at least one quaternary carbon atom is involved; also that additivity holds quite accurately for the cases given in Table 2 where the branches were separated.

Olefins.—In simple olefins there are two additional types of structures present, C–C=C and H–C=C; let their second-order perturbation energies be d and e respectively. Attention need be focused only on the effect of substitution at the double bond; the CH_2 increment here, as in all homologous series, is known to be constant for extension of a saturated chain. (This conclusion follows from the considerations in the previous section.) Table 4 gives the calculated total second-order perturbation energies (δE) and the corresponding energies (ΔE) that must be ascribed to the C=C bonds in order to use the empirical single bond energies in equation (3). It shows interesting regularities which can be summarized in the expression:

$$\Delta E = \Delta E_0 + (\text{no. of alkyl groups attached to C=C})(c - a + d - e) + (\text{no. of branches})(a - 2b + c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where ΔE_0 is the value of ΔE for ethylene. The correction for branching in the carbon skeleton is the same as for paraffins [compare equations (5) and (6)]. Since the branching factors are similar, a still simpler expression can be given for the heat of hydrogenation (ΔH) of an olefin to a paraffin, namely,

$$\Delta H = \Delta H_0 + A\ (\text{no. of alkyl substituents}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where ΔH_0 is the value of ΔH for ethylene and A is a constant.

The data in the third and seventh columns of Table 5 (Kistiakowsky *et al.*, *ibid.*, 1935, **57**, 65, 876; 1936, **58**, 137, 146; 1937, **59**, 831) show only a moderate agreement with equation (9).

TABLE 5. *Calculated and observed heats of hydrogenation of olefins, in kcal./mole.*

Olefin	H (Obs.)	$(H_0 - H)$ (Obs.)	$(H_0 - H)$ (Calc.)	Olefin	H (Obs.)	$(H_0 - H)$ (Obs.)	$(H_0 - H)$ (Calc.)
$CH_2{:}CH_2$	32·58	—	—	Me·CH:CH·Me-*trans*	27·62	4·96	5·0
Me·CH:CH_2	30·12	2·46		Me·CH:CH·Me-*cis* ...	28·57	4·01	4·0
Et·CH:CH_2	30·34	2·34		*cyclo*Hexene	28·59	3·99	
C_5H_{11}·CH:CH_2	30·14	2·44	2·5	$Me_2C{:}CHMe$	26·92	5·66	5·7
Pr^i·CH:CH_2	30·33	2·26		$Me_2C{:}CMe_2$	26·63	5·95	6·4
Bu^t·CH:CH_2	30·34	2·24					
$Me_2C{:}CH_2$	28·34	4·24					
MeEtC:CH_2	28·49	4·09	4·2				
$MePr^iC{:}CH_2$	28·00	4·58					

However, there are two factors which have so far been neglected. First, there is the steric repulsion between pairs of *cis*-alkyl groups, which is known to be important and accounts for the greater stability of *trans*-but-2-ene when compared with the *cis*-isomer; secondly, there is the tacit assumption that the interactions H–C–H, H–C–C, and C–C–C have the same value regardless of the stereochemistry of the central carbon atom. It is evident that the overlap and so the mutual interaction of these bonds will be less when the bond angle is 120° (in an olefin) than when it has the normal tetrahedral value (in a paraffin). Both these effects will stabilise the paraffin relatively to the olefin. Consequently a correction should be applied to ΔH for each pair of *cis*-alkyl groups, and a second correction for each pair of vicinal alkyl groups. Setting these corrections equal to 1 and 0·8 kcal./mole respectively, and the constant A in equation (9) equal to 2·5 kcal., we obtain the calculated values for ΔH given in the fourth and last column of Table 5. The agreement with experiment could hardly be better.

Other Bonds.—Consider a bond between carbon and some other element X. Denote the second-order perturbations for the groupings C–C–X, H–C–X by f, g respectively. The total second-order perturbation energies for RX with R = methyl, ethyl, *iso*propyl, and *tert.*-butyl are given in the second column of Table 6; and the corresponding second-order perturbation

TABLE 6. *Perturbation energies for* C–X *bonds.*

Compound	Total second-order perturbation	C–X bond perturbation
CH_3X	$3c + 3f$	$3g - \frac{1}{4}(-3a + 6b + 3c)$
$CH_3{\cdot}CH_2X$	$5b + 4c + f + 2g$	$f + 2g - \frac{1}{4}(a + 2b - 3c)$
$(CH_3)_2CHX$	$a + 8b + 6c + 2f + g$	$2f + g - \frac{1}{4}(a + 6b - c)$
$(CH_3)_3CX$	$3a + 9b + 9c + 3f$	$3f - \frac{1}{4}(-3a + 18b - 9c)$

energies that must be included in the C–X bond energy to give additivity are given in the last column. Since extension of the carbon chain at a β-carbon will not affect the C–X bond, these values for the C–X bond are appropriate to methyl, primary alkyl, secondary alkyl, and tertiary alkyl derivatives respectively. Although the expressions look complicated they actually show quite marked regularities. The empirical C–X bond energy (E_{CX}) is given by

$$E_{CX} = E^\circ_{CX} + A(a - 2b + c) + (\text{no. of β-alkyl groups})(f - g - b + c) \quad . \quad (10)$$

where $E°_{CX}$ is the value of E_{CX} for CH_3X, and A is a measure of chain-branching in the corresponding paraffin, being zero for methyl, one for ethyl or *iso*propyl, and two for *tert.*-butyl. The co-factor of A is the same as in the branching term of equation (6).

Equation (10) predicts that there should be a steady increase or decrease in the apparent C–X bond energy along the series, with, superimposed, an increase in bond energy of about 1·3 kcal. on passing from methyl to ethyl and from *iso*propyl to *tert.*-butyl. The latter effect does not appear if one allows specifically for branching; but it should do so in the conventional treatment. The most important point is that the apparent C–X bond energy will be a function of the number of β-carbon atoms; the values appropriate to primary, secondary, and tertiary Alkyl–X should differ, and primary Alkyl–X should differ from CH_3–X.

The branching factor can be eliminated by comparing the heats of formation of the hetero-compounds with those of corresponding paraffins.

The heat (ΔH) of formation (from atoms) of R_3CX, and the corresponding value (ΔH_0) for the paraffin R_3CH, are related by

$$\Delta H - \Delta H_0 = E_{CX} - E_{CH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where E_{CX} is the apparent C–X bond energy, and E_{CH} the C–H bond energy. The value for the apparent bond energy between carbon and a hetero-atom should according to the present treatment be given by

$$E_{CX} = (E_{CX})_0 + nA \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where $(E_{CX})_0$ is the value of E_{CX} for the methane derivative, and n is the number of carbon atoms adjacent to the C–X bond. In the case of carbonyl compounds, the comparison will be between R_2CO and R_2CH_2.

Reliable data are scanty, and the available information is summarised in Table 7. In practice heats of combustion have been used in place of heats of formation; the differences

TABLE 7. *Deviations from additivity of the heats of combustion of alcohols and carbonyl compounds.*

Compound	n	H	H_0	$H_0 - H$		Compound	n	H	H_0	$H_0 - H$	
MeOH	0	182·6	215·4	32·8		CH_2O	0	134·7	215·4	80·7	
EtOH	1	336·8	372·8	36·0		Me·CHO ...	1	284·7	372·8	88·1	
Pr^nOH	1	493·3	530·2	36·9	Mean	Me_2CO ...	2	434·6	530·2	95·6	
Bu^nOH ...	1	650·0	687·7	37·7	37·0	Et_2CO	2	746·8	845·1	98·3	Mean
Bu^iOH ...	1	649·3	686·4	37·1		$MePr^iCO$ ...	2	744·9	843·8	98·9	97·5
Pr^iOH	2	489·3	530·2	40·7		Pr^i_2CO ...	2	1059·9	1157·3	97·4	
Bu^tOH ...	3	643·3	686·4	43·1							

between these will differ from ($\Delta H - \Delta H_0$) for a given series of compounds only by a constant term. The final column gives these differences; and it will be seen that they vary linearly with n, as equation (12) requires.

DISCUSSION

In the preceding pages the following conclusions have been reached: (*a*) Interactions between bonds, and the consequent delocalisation of electrons, do not alter total binding energies to a first approximation. (*b*) The second-order interactions are functions of neighbouring bonds in unconjugated systems; they can to a large extent be absorbed into empirical bond energies. In homologous series the compensation can be perfect. The heats of formation of such compounds are linear functions of the numbers of carbon atoms to a very good approximation since the deviations are third-order quantities and usually quite negligible.

Conclusion (*b*) depends on the assumption that the important interactions are nearest-neighbour interactions, and not the 1 : 3 interactions of conventional hyperconjugation * (Mulliken, Rieke, and Brown, *ibid.*, 1941, **63**, 41). Platt (*loc. cit.*) showed that 1 : 3 interactions could not be important if the very accurate thermochemical data on paraffins were to be interpreted satisfactorily; and Altmann (*Proc. Roy. Soc.*, 1951, *A*, **210**, 327, 343) has given reasons for believing that the "conjugation" of alkyl groups with adjacent double bonds is a nearest-neighbour effect. One might add in this connexion that the chemical and spectroscopic evidence suggests strongly that all alkyl groups have a similar

* But see Appendix B.

and quite large conjugative effect when attached to unsaturated systems; the differences between different alkyl groups are relatively very small. This point is illustrated by the examples given in Table 7. In each case alkyl groups have a large effect, while the differences between different alkyl groups are very much smaller. Yet these cases are cited by Baker (" Hyperconjugation," Oxford Univ. Press, 1952, pp. 37, 44, 50) as good evidence for the importance of hyperconjugation in organic chemistry. We feel that these differences, which are undoubtedly due to hyperconjugation, are better regarded as small second- or third-order effects, and that the main electromeric effects of alkyl groups have some other origin. The main effect of alkyl groups cannot be inductive in nature since inductive effects would not alter heats of formation appreciably. A direct conjugation between adjacent bonds seems the most likely explanation. None of the regularities noted in Table 1 would follow were 1 : 3 interactions included, if only because such interactions would depend on the detailed stereochemistry of the molecule.

According to the views presented here the electrons in unconjugated molecules need not be localised. The additivity of bond energies is ascribed to the vanishing of the net first-order interactions between bonds, and to the possibility of absorbing second-order effects into empirical bond energies. The second-order contribution of a given bond is not, however, a function of that bond only, but depends also on its environment (*i.e.*, the number and kind of adjacent bonds). Strict additivity of bond energies would be expected only in compounds where the environments of the bonds are similar. In the general case it should be necessary to use a different value for the bond energy of a given bond for each different environment, corresponding to the different second-order perturbations that must be absorbed. This situation is recognised in the case of the carbonyl bond. Pauling (" The Nature of the Chemical Bond," Cornell Univ. Press, New York, 1941) gives three different values, corresponding to formaldehyde, other aldehydes, and ketones. But the same should be true of other bonds; and certainly the heats of formation of adjacent C–O or C–F bonds appear to be abnormally large. For instance, the heats of formation of acetals are uniformly 10—14 kcal. greater than those predicted from Pauling's bond energies (Dewar, *Trans. Faraday Soc.*, 1946, **42**, 767); and compounds of the type R_2CF_2 are abnormally stable.

One could in principle look at this problem from a different point of view. One could calculate heats of formation from " ideal " bond energies appropriate to localised bonds and describe the differences between the calculated and the observed heats of formation as resonance energies. This, of course, is the conventional view in the case of olefins where the differences between apparent heats of formation of the C=C bond are ascribed to hyperconjugation. However, similar differences appear in the case of saturated compounds, probably for similar reasons; the effects in olefins and saturated compounds are probably due in each case to interactions between adjacent bonds. The differences in heats of formation are also quite similar; the total range in apparent C=C bond energy in passing from ethylene to tetramethylethylene is about 6 kcal., virtually identical with the average difference in bond energy of the C–O bond between simple ethers and acetals, and much less than the corresponding difference between methanol and *tert.*-butyl alcohol. We have not discussed the values of the interaction terms that arise in this treatment, and experimental data are insufficient to allow them to be evaluated individually. The sign of the branching term in paraffins shows that $(a + c) > 2b$, but otherwise the signs and magnitudes of a, b, and c are indeterminate. Altmann's work (*loc. cit.*) suggests that a is in fact the dominant term in hydrocarbons, and all our results would be consistent with the assumption that interactions with bonds containing hydrogen can be neglected.

Appendix A.

In applying perturbation theory to sets of degenerate orthogonal unperturbed eigenfunctions it is usually necessary to replace each set of degenerate eigenfunctions by an appropriate set of linear combinations of those eigenfunctions, the linear combinations being found by first-order perturbation theory; the combinations are then used as a basis in calculating the second-order perturbations. If, however, only the sum of all the second-order perturbations of a degenerate set of eigenfunctions is required, it is legitimate to calculate them by using the original unper-

turbed eigenfunctions and by omitting terms with vanishing denominators. Only second-order perturbations by eigenfunctions extraneous to the set need be considered, for, as has been pointed out above, the sum of all mutual perturbations of eigenfunctions of the set by one another vanishes.

The theorem need be proved only for the most general case, *viz.*, the total second-order perturbation of one degenerate set of eigenfunctions by a second degenerate set. Denote the two sets by ϕ_r, ψ_s. Let the correct linear combination of these eigenfunctions found by first-order perturbation theory, *i.e.*, Φ_m, Ψ_n, be given by

$$\Phi_m = \sum_r a_{mr}\phi_r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$\Psi_n = \sum_s b_{ns}\psi_s \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

Let the energies of the various orbitals be

$$\text{of } \phi_m,\ E_m;\ \text{ of } \psi_n,\ F_n;$$
$$\text{of } \Phi_m,\ E_m + \varepsilon_m;\ \text{ of } \Psi_n,\ F_n + \zeta_n$$

where ε_m, ζ_n are first-order perturbations. It has been shown that

$$\sum_m \varepsilon_m = \sum_n \zeta_n = 0$$

The total second-order perturbation, ΔE, to the first set of levels, due to a perturbation operator P, is then given by

$$\Delta E = \sum_m \sum_n \Delta E_{mn} = \sum_m \sum_n \frac{\left[\int \Phi_m \cdot P \cdot \Psi_n \cdot d\tau\right]^2}{(E_m + \varepsilon_m) - (F_n + \zeta_n)} \quad . \quad . \quad . \quad . \quad . \quad (15)$$

$$\simeq \sum_m \sum_n \sum_r \sum_s \frac{a^2_{mr} \cdot b^2_{ns} \cdot P^2_{rs}}{E_m - F_n} + o(P^2\varepsilon,\ P^2\zeta)$$

where $$P_{rs} = \int \phi_r \cdot P \cdot \psi_s d\tau$$

Thus to the second-order of small quantities, *i.e.*, to the approximation of second-order perturbation theory,

$$\Delta E = \sum_m \sum_n \sum_r \sum_s \frac{a^2_{mr} b^2_{ns} P^2_{rs}}{E_m - F_n} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

Now if the functions ϕ_r are represented by unit orthogonal vectors in a many-dimensional space, equation (13) expresses the vector representing the function Φ_m in terms of the ϕ_r; the a_{mr} are then direction cosines relating Φ_m to the ϕ_r and the Φ_m form a set of unit orthogonal vectors related to the ϕ_r by (13). It follows at once (cf. Coulson and Rushbrooke, *Proc. Camb. Phil. Soc.*, 1940, **36**, 193, to whom this argument is due) that

$$\sum_m a^2_{mr} = \sum_r a^2_{mr} = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

Likewise $$\sum_n b^2_{ns} = \sum_s b^2_{ns} = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

Combining equations (16), (17), and (18) and carrying out the summation over m and n, we get

$$\Delta E = \sum_r \sum_s \frac{P^2_{rs}}{E_m - F_n}$$

But this is just the second-order perturbation to the ϕ_r's that would be calculated by using the unperturbed function ϕ_r, ψ_s as a basis, and by neglecting terms representing mutual perturbations of the ϕ_r (which would have vanishing denominators).

Further Refinement of the Treatment.—Although the whole of this treatment has been given in terms of the simple L.C.A.O. M.O. theory, it will be noticed that nowhere in it are simple L.C.A.O. M.O. wave functions or orbital energies. It is evident that the treatment would be quite unaffected if the bond orbitals used as a basis were ideal Hartree–Fock functions. The only approximation made has been the neglect of overlap between different bonds, apart, of course, from those inherent in the use of perturbation methods. Furthermore, the treatment would remain unaffected if the best possible two-electron wave functions were used for the

individual bonds, the " antibonding orbitals " now being replaced by two electron wave functions for excited states of the bond.

It is evident therefore that the simplifying assumptions inherent in the present treatment are much less restrictive than those made in current treatments of molecular structure, although for convenience we have formulated it in more familiar terms.

Appendix B.

Hyperconjugation is usually assumed to be important only if it involves C–H bonds. In this sense hyperconjugation cannot account for the phenomena we have discussed. If, however, hyperconjugation is of comparable importance for bonds of different types, so that the effect on a given C–C bond in hydrocarbon depends only on the number of adjacent carbon atoms, and not on the groups attached to those atoms, hyperconjugation could replace the adjacent bond interactions postulated in our treatment. In that case, in a hydrocarbon, the H–C–C and H–C–H interactions would be small, and only the C–C–C interaction significant. It is easily seen that none of our conclusions would be affected by this alternative interpretation.

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Queen Mary College, Mile End Road, London, E.1. [*Received, October 15th*, 1953.]

Addition of Free Radicals to Unsaturated Systems. Part VIII. The Direction of Radical-addition to Alkyl- and Perfluoroalkyl-acetylenes.*

By K. Leedham and R. N. Haszeldine.

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The photochemical reaction of trifluoroiodomethane with the compounds $RC{:}CH$ yields only $CF_3{\cdot}[CH{:}CR]_n{\cdot}CH{:}CRI$, where $R = CF_3$, C_2F_5, or CH_3, and $n = 1$ or 2. Heptafluoroiodopropane similarly reacts with trifluoromethylacetylene to give $C_3F_7{\cdot}[CH{:}C{\cdot}(CF_3)]_n{\cdot}CH{:}CI{\cdot}CF_3$. The rate but not the direction of addition of the perfluoroalkyl radical to an acetylene $RC{:}CH$ is affected by the inductive effect of R. Alternative syntheses for $CF_3{\cdot}CH{:}CH{\cdot}CF_3$ and $CF_3{\cdot}CH{:}CH{\cdot}CH_3$, and ultra-violet and infra-red spectra are reported.

In attempting to determine how the direction of addition of a radical to an unsaturated system is influenced by the substituents on the unsaturated system, olefins of the type $RCH{:}CH_2$ were studied in Part II (Haszeldine and Steele, *J.*, 1953, 1199). The present communication describes a similar study with acetylenes, $RC{:}CH$. The perfluoroalkyl radicals CF_3 and C_3F_7 were used, prepared by the photolysis of the corresponding fluoroalkyl iodide, and the reasons for the choice of such radicals, and the assumptions made, have been stated earlier (*J.*, 1952, 2504).

Trifluoromethylacetylene and trifluoroiodomethane do not react at room temperature in the absence of light. The photochemical reaction proceeds smoothly and with liberation of only small amounts of iodine. The 1 : 1 addition product could be (I) or (II), but replacement of its iodine atom by hydrogen by means of zinc and hydrochloric acid gives a high yield of the known *trans*-hexafluorobut-2-ene (III) which can be derived only from (I).

$CF_3{\cdot}CH{:}CI{\cdot}CF_3$	$(CF_3)_2C{:}CHI$	$CF_3{\cdot}CH{:}CH{\cdot}CF_3$	$(CF_3)_2C{:}CH_2$
(I)	(II)	(III)	(IV)

The infra-red spectrum of the reduction product establishes the *trans*-configuration, and shows that the known hexafluoro*iso*butene (IV), which would have been obtained from (II), is not formed. It is noteworthy that the zinc–hydrochloric acid reduction is stereospecific.

* Part VII, Haszeldine and Steele, *J.*, 1954, 923.

The 1 : 1 addition product is thus 1 : 1 : 1 : 4 : 4 : 4-hexafluoro-2-iodobut-2-ene (I), formed by a chain reaction of the type postulated earlier :

$$CF_3I \xrightarrow{h\nu} CF_3\cdot + I\cdot$$
$$CF_3\cdot + CF_3\cdot C{:}CH \longrightarrow CF_3\cdot \dot{C}{:}CH\cdot CF_3$$
$$CF_3\cdot \dot{C}{:}CH\cdot CF_3 + CF_3I \longrightarrow CF_3\cdot CI{:}CH\cdot CF_3 + CF_3\cdot \longrightarrow \text{etc.}$$

The 1 : 1 adduct has the same constitution whether light which only trifluoroiodomethane can absorb (>3000 Å) or light which both fluoro-iodide and acetylene can absorb (>2200 Å) is used to initiate the reaction; the reaction under the former conditions (Pyrex vessels) is appreciably slower than when the latter conditions (silica vessels) are used.

A 1 : 2 addition product is also formed by the reaction of trifluoroiodomethane with trifluoromethylacetylene. That this is (V) or (VI), and not (VII) or (VIII), is shown by analytical and spectroscopic results. A compound such as (VII) would be formed by addition of trifluoroiodomethane to (I), and a compound such as (VIII) would be obtained by the not improbable combination of two resonance-stabilised $CF_3\cdot CH{:}\dot{C}\cdot CF_3$ radicals, followed by addition of trifluoroiodomethane to the resultant tetrakistrifluoromethylbutadiene. The absence of compounds such as (VIII) illustrates the efficiency of the chain transfer and, to a lesser extent, the propagation steps, in the reaction mechanism. Since the 1 : 1 addition product is 1 : 1 : 1 : 4 : 4 : 4-hexafluoro-2-iodobut-2-ene, the trifluoromethyl radical must

$CF_3\cdot CH{:}C(CF_3)\cdot CH{:}CI\cdot CF_3$ (V)

$CF_3\cdot CH{:}C(CF_3)\cdot C(CF_3){:}CHI$ (VI)

$(CF_3)_2CH\cdot CI_2\cdot CF_3$ (VII)

$CF_3\cdot CH{:}C(CF_3)\cdot C(CF_3)_2\cdot CHI\cdot CF_3$ (VIII)

attack the :CH in trifluoromethylacetylene to give $CF_3\cdot CH{:}\dot{C}\cdot CF_3$; the attack of this radical on a second molecule of the acetylene will also occur at the :CH carbon atom, so that the propagation step is

$$CF_3\cdot CH{:}\dot{C}\cdot CF_3 + CF_3\cdot C{:}CH \longrightarrow CF_3\cdot CH{:}C(CF_3)\cdot CH{:}\dot{C}\cdot CF_3, \text{ etc.}$$

followed by the chain-transfer step

$$CF_3\cdot CH{:}C(CF_3)\cdot CH{:}\dot{C}\cdot CF_3 + CF_3I \longrightarrow CF_3\cdot CH{:}C(CF_3)\cdot CH{:}CI\cdot CF_3 + CF_3\cdot$$

The 1 : 2-adduct is thus very probably 1 : 1 : 1 : 6 : 6 : 6-hexafluoro-2-iodo-4-trifluoromethylhexa-2 : 4-diene (V) and not (VI). As will be reported later, (V) can be converted into 1 : 2 : 4-tristrifluoromethylbutadiene.

Trifluoroiodomethane similarly reacts smoothly with pentafluoroethylacetylene to give 1 : 1 and 1 : 2 addition products. The constitutions of these products are assumed to be (IX) and (X) by analogy with the reactions with trifluoromethylacetylene.

$CF_3\cdot CH{:}CI\cdot C_2F_5$ (IX) $CF_3\cdot CH{:}C(C_2F_5)\cdot CH{:}CI\cdot C_2F_5$ (X) $C_3F_7\cdot CH{:}CI\cdot CF_3$ (XI) $C_3F_7\cdot CH{:}C(CF_3)\cdot CH{:}CI\cdot CF_3$ (XII)

Attack on trifluoromethylacetylene proceeds as smoothly with a heptafluoropropyl as with a trifluoromethyl radical, and (XI) and (XII), the analogous products to (I) and (V), are obtained; their assumed constitution is supported by their spectra (see Table).

The photochemical reaction of trifluoroiodomethane with methylacetylene is much more rapid than with trifluoromethylacetylene. There is no dark reaction, and only slight attack on the methyl group to give the $\dot{C}H_2\cdot C{:}CH$ radical during the photochemical reaction, since only very small amounts of fluoroform could be detected. High yields of a 1 : 1 and what is probably a 1 : 2 addition product were obtained, and spectroscopic examination showed that the 1 : 1 adduct was the same whether Pyrex or silica vessels were used. The 1 : 1 adduct is (XIII), since the iodine atom can be replaced by hydrogen in high yield to give only the known 1 : 1 : 1-trifluorobut-2-ene (XV); infra-red spectroscopic examination shows that the isomeric trifluoro*iso*butene (XVI), b. p. 6·4°, is absent. This compound would have been formed if trifluoroiodomethane addition to propyne had taken place in the

opposite sense to that shown by (XIII). Attack of the trifluoromethyl radical is thus exclusively on the :CH carbon atom of propyne with a reaction mechanism similar to that for the perfluoroalkylacetylenes given above. The 1 : 2-addition product will have the constitution shown by (XIV).

$CF_3{\cdot}CH{:}CI{\cdot}CH_2$ (XIII) $CF_3{\cdot}CH{:}C(CH_3){\cdot}CH{:}CI{\cdot}CH_3$ (XIV) $CF_3{\cdot}CH{:}CHMe$ (XV) $CF_3{\cdot}CMe{:}CH_2$ (XVI)

The vinylic C–H and the C:C stretching vibrations in the infra-red, and the ultra-violet spectra of certain of the above compounds, are shown in the Table. The C:C stretching absorption in the substituted butadienes is doubled, indicating *cis–trans*-isomerism about one or both of the double bonds; the vinylic C–H absorption appears at its characteristic wave-length. The ultra-violet absorption of compounds of the type $R_F{\cdot}CH{:}CI{\cdot}R_F$ is characteristic, and sufficiently different from that of compounds $R_F{\cdot}CH{:}CI{\cdot}Alk$ (where R_F = perfluoroalkyl) to be used diagnostically.

Discussion.—The reaction of HX (X = F, Cl, or Br) with propyne under conditions favouring ionic intermediates yields only compounds $CH_3{\cdot}CX{:}CH_2$, *i.e.*, propyne is polarised as $CH_3{\cdot}\overset{\delta+}{C}{\equiv}\overset{\delta-}{C}H$ in such reactions. By contrast, trifluoromethylacetylene reacts with HX (X = F, Cl, Br, I, OMe, OEt, or NR_2) to give $CF_3{\cdot}CH{:}CHX$ (*J.*, 1952, 3490), *i.e.*, is polarised as $CF_3{\cdot}\overset{\delta-}{C}{\equiv}\overset{\delta+}{C}H$. As shown above, free-radical attack on these acetylenes is *exclusively* on the terminal carbon atom, *i.e.*, the *direction* of free-radical attack on a terminal acetylene is independent of the inductive or hyperconjugative effects of R in R·C:CH, since these act in opposite directions when R = CH_3 and R = CF_3. The apparent polarisation of the triple bond does affect markedly, however, the *rate* of reaction; the rate is much greater when R = CH_3 than when R = CF_3.

	Infra-red		Ultra-violet spectra (in light petroleum)			
	C–H	C:C	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$
$CF_3{\cdot}CH{:}CI{\cdot}CF_3$, b. p. 75·5° ...	3·25μ	6·00, 6·07, 6·14 triplet	243 222	3250 4250	236 —	3150 —
$CF_3{\cdot}CH{:}CI{\cdot}C_2F_5$, b. p. 85°.....	3·27	6·07	248 226	3000 4000	240 —	2900 —
$C_2F_7{\cdot}CH{:}CI{\cdot}CF_3$, b. p. 110° ...	3·25	6·06	248 226	3450 4400	240 —	3250 —
$CF_3{\cdot}CH{:}CI{\cdot}CH_3$, b. p. 94·5° ...	3·24	6·07	260 230 215	350 3800 3500	251·5 221·5 —	320 3100 —

		Infra-red bands (μ)	
Compound	B. p./mm.	C–H	C:C
(V)	60°/77	3·25	5·90, 6·10
(X)	87/100	3·25	5·94, 6·16
(XII)	75/70	3·25	5·92, 6·10
(XIV)	55/7	3·24	6·03, 6·23

It was shown earlier that the photochemical reaction of hydrogen bromide with trifluoromethylacetylene gave only 1-bromo-3 : 3 : 3-trifluoropropene (*J.*, 1952, 3490); Kharasch, McNab, and McNab (*J. Amer. Chem. Soc.*, 1935, **57**, 2463) showed that the " peroxide effect " in the reaction of hydrogen bromide with propyne gave 1 : 2-dibromopropane. In both reactions, the initial attack of the bromine atom is thus directed in the same way as a free perfluoroalkyl radical:

$$Br{\cdot} + RC{:}CH \longrightarrow R\dot{C}{:}CHBr \xrightarrow{HBr} RCH{:}CHBr + Br{\cdot}, \text{ etc.}$$

Bader, Cross, Heilbron, and Jones (*J.*, 1949, 619) showed that radical attack during the peroxide-induced reaction of thiolacetic acid with monosubstituted acetylenes was on the terminal carbon atom of the alkyne. The trichloromethyl radical from trichloroiodomethane also attacks the terminal carbon atom in 3 : 3 : 3-trifluoropropyne (Haszeldine, *J.*, 1953, 922):

$$CF_3{\cdot}C{:}CH + CCl_3I \xrightarrow{h\nu} CF_3{\cdot}CI{:}CH{\cdot}CCl_3$$

Free-radical attack on propyne and trifluoromethylacetylene is thus very similar to the corresponding reactions with propylene and 3 : 3 : 3-trifluoropropene (*J.*, 1952, 2504; 1953, 1199) where attack is exclusively on the terminal CH_2 group. It can be concluded that the intermediate free radicals R'H·C·CR are more stable than the radicals RR'C·CH, but a full discussion is deferred, as with the results of papers presented earlier in this series, to a paper in course of preparation.

Experimental

Trifluoroiodomethane (*J.*, 1951, 584), trifluoromethylacetylene (*J.*, 1951, 588, 2495; 1952, 3483), pentafluoroethylacetylene (*J.*, 1952, 3483), and heptafluoroiodopropane (*J.*, 1949, 2886) were thoroughly dried and stored in a vacuum system. Reactions were carried out in sealed 50-ml. Pyrex or silica tubes, with exclusion of moisture, oxygen, etc., which might catalyse ionic or free-radical reactions. A Hanovia lamp was used as source of ultra-violet radiation.

Reaction of Trifluoroiodomethane with 3 : 3 : 3-*Trifluoropropyne.*—Trifluoroiodomethane (4·0 g., 0·02 mole) and 3 : 3 : 3-trifluoropropyne (1·92 g., 0·02 mole) in a silica tube were exposed to ultra-violet light for 72 hr. with the liquid phase shielded from light. The small amount of iodine which had been liberated was removed by treatment with mercury, and the liquid products were distilled to give 1 : 1 : 1 : 4 : 4 : 4-*hexafluoro*-2-*iodobut*-2-*ene* (2·22 g., 38%), b. p. 75·5° (isoteniscope), n_D^{16} 1·3758 (Found : C, 16·4; H, 0·6%; *M*, 288. C_4HIF_6 requires C, 16·6; H, 0·4%; *M*, 290), and material of higher b. p. The latter was distilled through a small column, to give 1 : 1 : 1 : 6 : 6 : 6-*hexafluoro*-2-*iodo*-4-*trifluoromethylhexa*-2 : 4-*diene* (0·7 g., 9%), b. p. 60°/77 mm. (Found : C, 22·0; H, 0·7. $C_7H_2IF_9$ requires C, 21·9; H, 0·5%).

Irradiation of trifluoroiodomethane and 3 : 3 : 3-trifluoropropyne in a Pyrex tube for 10 days also gave 1 : 1 : 1 : 4 : 4 : 4-hexafluoro-2-iodobut-2-ene, shown to be identical with the compound obtained above by comparison of infra-red spectra.

Reduction of 1 : 1 : 1 : 4 : 4 : 4-*Hexafluoro*-2-*iodobut*-2-*ene.*—The compound (0·69 g.) was added dropwise (30 min.) to zinc dust (10 g.) and 10% hydrochloric acid (12 ml.) in a flask fitted with reflux condenser connected *via* rubber tubing to a trap cooled in liquid oxygen. The reactants were heated at 60° for 1·5 hr., with intermittent addition of concentrated hydrochloric acid (2 ml.). The gaseous contents of the flask were swept out with nitrogen, and the combined volatile products were fractionated to give *trans*-1 : 1 : 1 : 4 : 4 : 4-hexafluorobut-2-ene (0·27 g., 70%), b. p. (isoteniscope) 9·1° (Found : *M*, 165. Calc. for $C_4H_2F_6$: *M*, 164), identified by comparison of its b. p. and infra-red spectrum with those reported earlier (*J.*, 1952, 2504).

In a second experiment, magnesium (1 g.) was added to the zinc (15 g.) used for the reduction of the iodo-compound (1·97 g.); the yield of *trans*-hexafluorobut-2-ene was 78%.

Reaction of Pentafluoroethylacetylene with Trifluoroiodomethane.—The acetylene (2·54 g., 0·02 mole)and trifluoroiodomethane (3·46 g., 0·02 mole) were sealed in a silica tube and irradiated for 71 hr., affording unchanged trifluoroiodomethane and liquid products which were distilled to give 1 : 1 : 1 : 4 : 4 : 5 : 5 : 5-*octafluoro*-3-*iodopent*-2-*ene* (1·69 g., 29%), b. p. 84—86°, n_D^{16} 1·3623 (Found : C, 17·9; H, 0·6%; *M*, 338. C_5HIF_8 requires C, 17·6; H, 0·3%; *M*, 340), and 1 : 1 : 1 : 6 : 6 : 7 : 7 : 7-*octafluoro*-5-*iodo*-3-*pentafluoroethylhepta*-2 : 4-*diene* (*ca.* 0·3 g., 4%), b. p. 86—88°/100 mm. (Found : C, 22·4; H, 0·8. $C_9H_2IF_{13}$ requires C, 22·3; H, 0·4%).

Reaction of Heptafluoroiodopropane with 3 : 3 : 3-*Trifluoropropyne.*—Heptafluoroiodopropane (23·3 g., 0·088 mole) and 3 : 3 : 3-trifluoropropyne (4·72 g., 0·033 mole) were irradiated in a Pyrex tube for 13 days. Distillation gave unchanged heptafluoroiodopropane (8·16 g., 35%), 1 : 1 : 1 : 4 : 4 : 5 : 5 : 6 : 6 : 6-*decafluoro*-2-*iodohex*-2-*ene* (8·90 g., 38%), b. p. 110°, n_D^{13} 1·3575 (Found : C, 18·6; H, 0·4. C_6HIF_{10} requires C, 18·5; H, 0·2%), and 1 : 1 : 1 : 6 : 6 : 7 : 7 : 8 : 8 : 8-*decafluoro*-2-*iodo*-4-*trifluoromethylocta*-2 : 4-*diene* (*ca.* 1 g.), b. p. 83°/56 mm. (Found : C, 21·8; H, 0·4. $C_9H_2IF_{13}$ requires C, 22·3; H, 0·4%).

Reaction of Propyne with Trifluoroiodomethane.—In a typical experiment, trifluoroiodomethane (17·5 g., 0·089 mole), sealed in a silica tube with propyne (3·72 g., 0·093 mole), was exposed to ultra-violet light for 17 hr. with the liquid phase shielded from light, to give liquid products (18·2 g., 86%). These were distilled to give 1 : 1 : 1-*trifluoro*-3-*iodobut*-2-*ene* (16·2 g., 89%), b. p. 94·5°, n_D^{20} 1·4352 (Found : C, 20·2; H, 1·7. $C_4H_4IF_3$ requires C, 20·3; H, 1·7%), and a residue of higher b. p. Only traces of fluoroform were detected by infra-red spectroscopic examination. An experiment in a Pyrex tube also gave 1 : 1 : 1-trifluoro-3-iodobut-2-ene, shown to be identical with the compound prepared as above by comparison of infra-red spectra.

The products of higher b. p. from several experiments were combined and distilled to give

what is probably the 1 : 2 addition product, 1 : 1 : 1-trifluoro-5-iodo-3-methylhexa-2 : 4-diene, b. p. 54—55°/7 mm.

Blank experiments in which propyne was irradiated alone, or in presence of iodine, showed that it did not isomerise to allene.

Reduction of 1 : 1 : 1-*Trifluoro*-3-*iodobut*-2-*ene*.—The iodo-compound (2·10 g.) was added to zinc dust (15 g.), magnesium (1 g.), and 50% hydrochloric acid (20 ml.), kept at room temperature (5 hr.), then heated slowly to 100° (2 hr.). The volatile products passed through a reflux water-condenser, were collected in a trap cooled by liquid oxygen, and then distilled *in vacuo* to give 1 : 1 : 1-trifluorobut-2-ene (83%), b. p. (isoteniscope) 16·5° (Found: *M*, 110. Calc. for $C_4H_5F_3$: *M*, 110), and unchanged 1 : 1 : 1-trifluoro-3-iodobut-2-ene (0·16 g.). Apart from 1 : 1 : 1-trifluorobut-2-ene, there was no material boiling in the region 0—30°. The trifluorobutene was identified by comparison of the infra-red spectrum of its dichloride (prepared by reaction with chlorine in the dark) with that of the dichloride similarly prepared from a known specimen of 1 : 1 : 1-trifluorobut-2-ene, b. p. 20° (Haszeldine and Steele, *J.*, 1953, 1199).

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, December* 21*st*, 1953.]

Hydroxypyridine and Hydroxyquinoline Phosphates as Anti-cholinesterases.

By K. J. M. ANDREWS, F. R. ATHERTON, F. BERGEL, and A. L. MORRISON.

[Reprint Order No. 5012.]

Dialkyl phosphoric esters of hydroxypyridines and hydroxyquinolines have been prepared. The moderate anti-cholinesterase activity of these compounds is enhanced by conversion into the quaternary salts, only one of which was obtained crystalline.

In a previous paper (*J.*, 1952, 780) we described the preparation of phosphoric esters which structurally resembled "Prostigmin." Since the anti-cholinesterase activities of carbamates of 3-hydroxypyridinium salts have been reported on several occasions (Roche Products, B.P. 613,168; Blaschko, Bülbring, and Chou, *Brit. J. Pharmacol.*, 1949, **4**, 29; Wuest and Sakal, *J. Amer. Chem. Soc.*, 1951, **73**, 1210; Casier and Verbecke, *Arch. int. Pharmacodyn.*, 1950, **83**, 452), we have extended our work to the preparation of phosphoric esters of 3-hydroxypyridine and various hydroxyquinolines.

When the potassium or sodium salt of 3-hydroxypyridine reacted with diethyl or di*iso*propyl phosphorochloridate, oils were obtained which could be distilled in a high vacuum; reactions with ethyl *NN*-diethylphosphoramidochloridate and *NNP*-triethylphosphoramidic chloride gave similar products. Relevant data, including toxicities and inhibition of "true" cholinesterase *in vitro*, are given in the Experimental section.

Similarly, 3-, 4-, or 8-hydroxyquinoline, treated with diethyl phosphorochloridate, yielded the corresponding derivatives as distillable oils. Although 3-(di*iso*propoxyphosphinyloxy)quinoline could be made without difficulty, the dimethyl homologue decomposed on attempted high-vacuum distillation into a black resin. By analogy with the behaviour of the *m*-(dimethoxyphosphinyloxy)-*N*-dimethylaniline described in Part V (*loc. cit.*), we believe that betaine may have been formed.

All tertiary bases, with the exception of 3-(diethoxyphosphinyloxy)quinoline, failed to yield crystalline quaternary salts although a wide range of alkyl and aralkyl halides was employed: analyses of liquid methobromides showed them to be substantially the required compounds. When reactions with the halides were attempted above room temperature, the ether-insoluble oils produced contained very little ionisable halogen: this can only be interpreted as the formation of a betaine. Since we had shown that the tertiary bases were stable at those temperatures, this reaction must be represented as an anionic dealkylation similar to those observed by Clark and Todd (*J.*, 1950, 2031).

Crystalline 3-(diethoxyphosphinyloxy)-*N*-methylquinolinium methyl sulphate, desig-

nated Ro 3-0422, showed *in vitro* the highest anti-cholinesterase activity so far recorded in the literature for a phosphorus compound, namely I_{50} (red cell) $= 1{\cdot}5 \times 10^{-10}$. This value is over 300 times the potency of "Prostigmin" against "true" cholinesterase (Hobbiger, *Brit. J. Pharmacol.*, 1954, in the press); the toxicity was correspondingly high (by intravenous route in mice, $LD_{50} = 0{\cdot}023$ mg./kg.).

In view of its pharmacological interest, an investigation of its hydrolysis was carried out. A sample, stored at 25° in an atmosphere of 70% humidity for seven weeks, had lost nearly all its activity ($I_{50} = 2{\cdot}7 \times 10^{-7}$) and gave the same yield of picrate (m. p. 239—241°) as was obtained from an equivalent amount of 3-hydroxy-*N*-methylquinolinium methyl sulphate. Paper chromatography showed, as expected, that breakdown consisted of simple hydrolysis to diethyl hydrogen phosphate and 3-hydroxy-*N*-methylquinolinium methyl sulphate: with solvent systems (upper layers) of ethyl acetate : pyridine : water (100 : 45 : 100) and *tert.*-amyl alcohol : water : formic acid (3 : 3 : 1 and 2 : 2 : 1), aged material gave only two spots, showing R_F values identical with those of authentic samples. Since the products of hydrolysis have little anti-cholinesterase activity, the percentage hydrolysis of solutions of Ro 3-0422 could be estimated from their activity. The following results were obtained with 0·1% solutions:

	I_{50} (red cells)	Hydrolysis (%)		I_{50} (red cells)	Hydrolysis (%)
Fresh solution	$1{\cdot}5 \times 10^{-10}$	—	After 3 weeks at 20°	$3{\cdot}3 \times 10^{-10}$	55
After 3 weeks at 4°...	$2{\cdot}3 \times 10^{-10}$	33	After 3 weeks at 45°	$2{\cdot}5 \times 10^{-8}$	99·4

Experimental

3-(Diethoxyphosphinyloxy)pyridine (Ro 3-0346).—3-Hydroxypyridine (4·75 g.) was dissolved in a solution of sodium ethoxide prepared from metallic sodium (1·3 g.) and dry ethanol (80 ml.). Diethyl phosphorochloridate (9·75 g.) was added dropwise, with stirring, to the resultant solution during 15 min. The mixture was then boiled for 30 min. and then left overnight. Next day, the sodium chloride was filtered off and the fitrate evaporated in a vacuum. The residual oil was dissolved in carbon tetrachloride (*ca.* 40 ml.) and washed three times with 0·5N-sodium hydroxide and then with water. After being dried (Na_2SO_4), the solvent was evaporated and the residue distilled in a high vacuum, to yield 8·5 g. (73%) of *3-(diethoxyphosphinyloxy)pyridine* as a colourless oil, b. p. $82°/5{\cdot}8 \times 10^{-6}$ mm., n_D^{22} 1·4752 (Found: N, 6·1; P, 13·1. $C_9H_{14}O_4NP$ requires N, 6·1; P, 13·4%).

The following tertiary bases were prepared similarly:

3-(Diisopropoxyphosphinyloxy)pyridine (Ro 3-0351) (69%), b. p. $84°/1{\cdot}5 \times 10^{-4}$ mm., n_D^{22} 1·4687 (Found: N, 5·6; P, 11·9. $C_{11}H_{18}O_4NP$ requires N, 5·4; P, 12·0%).

3-[Diethylamino(ethoxy)phosphinyloxy]pyridine (Ro 3-0347) (84%), b. p. $87°/4 \times 10^{-3}$ mm., n_D^{22} 1·4852 (Found: N, 10·4; P, 11·7. $C_{11}H_{19}O_3N_2P$ requires N, 10·8; P, 12·0%).

3-[Diethylamino(ethyl)phosphinyloxy]pyridine (Ro 3-0352) (35%), b. p. $98°/2{\cdot}8 \times 10^{-4}$ mm., n_D^{22} 1·5030 (Found: N, 11·5; P, 12·0. $C_{11}H_{19}O_2N_2P$ requires N, 11·6; P, 12·8%).

3-(Diethoxyphosphinyloxy)quinoline (Ro 3-0419) (52%), b. p. $120—124°/1{\cdot}1 \times 10^{-5}$ mm., n_D^{21} 1·5360 (Found: N, 4·9; P, 10·7. $C_{13}H_{16}O_4NP$ requires N, 5·0; P, 11·0%).

3-(Diisopropoxyphosphinyloxy)quinoline (Ro 3-0433) (69%), b. p. $120—124°/2{\cdot}3 \times 10^{-5}$ mm. (Found: N, 4·7; P, 10·0. $C_{15}H_{20}O_4NP$ requires N, 4·5; P, 10·0%).

4-(Diisopropoxyphosphinyloxy)quinoline (Ro 3-0617) (37%), b. p. $112°/9{\cdot}2 \times 10^{-5}$ mm., n_D^{23} 1·5212 (Found: N, 4·5; P, 9·6. $C_{15}H_{20}O_4NP$ requires N, 4·5; P, 10·0%).

8-(Diethoxyphosphinyloxy)quinoline (Ro 3-0417) (57%), b. p. $133—137°/5{\cdot}2 \times 10^{-5}$ mm., n_D^{21} 1·5447 (Found: N, 5·1; P, 10·3. $C_{13}H_{16}O_4NP$ requires N, 5·0; P, 11·0%).

Ro	I_{50} (Red cells)	LD_{50} (mg./kg. mice, i.v.)
3–0346	5×10^{-7}	0·14; 0·4
,, (Methobromide)	2×10^{-8}	3·2
3–0351	1×10^{-6}	6·0
,, (Methobromide).....	*ca.* 5×10^{-9}	0·33
3–0347	*ca.* 1×10^{-5}	7·7
,, (Methobromide).....	$>1 \times 10^{-5}$	100
3–0352	—	75
,, (Methobromide).....	1×10^{-5}	75
3–0419	$2{\cdot}2 \times 10^{-8}$	1·0
3–0433	$7{\cdot}8 \times 10^{-8}$	—
3–0417	—	37
3–0422	$1{\cdot}5 \times 10^{-10}$	0·023

3-(*Diethoxyphosphinyloxy*)-N-*methylquinolinium Methyl Sulphate* (Ro 3-0422).—Methyl sulphate (0·75 ml.) was added to a solution of 3-(diethoxyphosphinyloxy)quinoline (1·4 g.) in dry benzene (5 ml.), and the mixture was kept at room temperature for 24 hr. The separated oil crystallised on trituration with ether, to give a solid, m. p. 105—107°. Recrystallisation by dissolving it in alcohol and adding dry ether to turbidity gave the *salt*, m. p. 109—110° (yield 72%). Two further crystallisations gave long, colourless needles, m. p. 111—112° (Found: N, 3·9; P, 7·3. $C_{15}H_{22}O_8NPS$ requires N, 3·4; P, 7·6%). The analogous *picrate*, prepared in aqueous solution, had m. p. 135—137° (softened at 108—110°) (Found: C, 46·2; H, 4·0. $C_{20}H_{21}O_{11}N_4P$ requires C, 45·8; H, 4·0%).

3-*Hydroxy*-N-*methylquinolinium Methyl Sulphate*.—Prepared from 3-hydroxyquinoline and methyl sulphate in alcohol at room temperature, this compound had m. p. 176—178° after two recrystallisations from alcohol and gave only one spot on a paper chromatogram (*n*-butanol–water–acetic acid, 10 : 7 : 3; Whatman No. 1 paper) (Found: C, 48·9; H, 5·0. Calc. for $C_{11}H_{13}O_5NS$: C, 48·7; H, 4·8%). The *picrate* prepared in aqueous solution had m. p. 239—241° (Found: C, 49·9; H, 3·1. $C_{16}H_{12}O_8N_4$ requires C, 49·5; H, 3·1%).

Cragoe, Robb, and Bealor (*J. Org. Chem.*, 1953, **18**, 552) give m. p. 163—165° for 3-hydroxy-*N*-methylquinolinium methyl sulphate. We found that when heat was applied in the preparation of this quaternary salt a lower m. p. product was obtained. A paper chromatogram showed the material to be non-homogeneous; the impurity preceded the main spot when the above solvent system was used.

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RESEARCH DEPARTMENT, ROCHE PRODUCTS LIMITED,
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Some Derivatives of 2-Phenylindane.

By P. C. JOCELYN.

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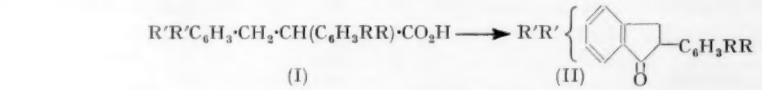
Some new methoxyphenyl-phenylpropionic acids have been prepared and attempts made to cyclise them to methoxy-2-phenylindanones. The latter, where obtained, have been converted into the corresponding 1-amino-*x*-methoxy-2-phenylindanes.

THE effect of cyclising reagents on a number of methoxyphenyl-phenylpropionic acids has been investigated as a route to the corresponding methoxy-2-phenylindan-1-ones.

β-Methoxyphenyl-α-phenylpropionic acids (I; R = H, R′,R′ = OMe, H or diOMe) were first synthesised in 60% yield by reduction with sodium amalgam of the corresponding cinnamic acids. Rather higher yields were however obtained by the sequence: (*a*) condensation of the requisite methoxybenzaldehydes with benzyl cyanide (cf. Frost, *Annalen*, 1888, **250**, 159), (*b*) smooth reduction of the resultant methoxyphenylcinnamonitriles (resistant to hydrolysis) to the propionitriles, and (*c*) ready hydrolysis of the propionitriles to the desired acids.

α-Methoxyphenyl-β-phenylpropionic acids (I; R,R = OMe, H or diOMe, R′ = H) were similarly produced from methoxybenzyl cyanides and benzaldehyde.



(I) (II)

αβ-Diphenylpropionic acid was not cyclised to 2-phenylindan-1-one by concentrated sulphuric acid (contrary to the report by von Miller and Rohde, *Ber.*, 1892, **25**, 2095) or by phosphoric oxide in benzene, but cyclisation was easily effected by phosphoric oxide–phosphoric acid (Koebner and Robinson, *J.*, 1938, 1994).

The action of this reagent on acids (I) is summarised in the Table.

Substituents in (I)		Optimum	Max.	Product (II),	
R,R	R′,R′	temp.	yield, %	R	R′
2H	*o*-OMe,H	—	none	—	—
2H	*m*-OMe,H	160°	40	2H	5-OMe,H
2H	*p*-OMe,H	187	20	2H	6-OMe,H
2H	3 : 4-di-OMe [1]	160	30	2H	5 : 6-diOMe
3 : 4-diOMe	3 : 4-di-OMe [2]	—	none	—	—
3 : 4-diOMe	2H	—	,,	—	—
p-OMe,H	2H	—	,,	—	—
m-OMe,H	2H	—	,,	—	—

[1] In contrast to the other acids, this was easily cyclised by phosphoric oxide in benzene. [2] Solmssen (*J. Amer. Chem. Soc.*, **1943**, **65**, 2370) has reported the cyclisation of (I; R,R = *p*-OMe,H, R′,R = *m*-OMe,H) with phosphoric oxide in benzene.

The methoxy-2-phenyl-1-indanones (II) thus obtained were converted *via* the oximes to the corresponding 1-amino-x-methoxy-2-phenylindanes.

During this work, 2-phenylindene was converted into 1-bromo-2-phenylindene with *N*-bromosuccinimide. Attempts to reduce this bromide to the dihydro-derivative led to the prior loss of bromine.

Experimental

m-*Methoxy-α-phenylcinnamonitrile.*—*m*-Methoxybenzaldehyde (55 g.), benzyl cyanide (50 g.), ethanol (150 c.c.) and 6N-sodium hydroxide solution (5 c.c.) were set aside for 12 hr. The precipitate was filtered off and dissolved in boiling ethanol, from which m-*methoxy-α-phenylcinnamonitrile* (90 g., 90%), m. p. 57°, crystallised on cooling (Found: C, 81·5; H, 5·5. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5%).

The following were prepared similarly: o-*Methoxy-α-phenylcinnamonitrile*, m. p. 94° (Found: C, 81·4; H, 5·5%), and α-m-*methoxyphenylcinnamonitrile*, m. p. 72° (Found: C, 82·1; H, 5·6%).

β-m-*Methoxyphenyl-α-phenylpropiononitrile.*—*m*-Methoxy-α-phenylcinnamonitrile (10 g.) was refluxed in ethanol (100 c.c.) with sodium amalgam (2½%; 100 g.) for 1 hr., the ethanol evaporated from the filtered solution, and the residue distilled, β-m-*methoxyphenyl-α-phenylpropiononitrile* (9·6 g., 95%) being collected at 140°/0·02 mm. (Found: C, 81·0; H, 6·4. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3%). The following were prepared similarly from the corresponding cinnamonitriles (Freund and Remse, *Ber.*, 1890, **23**, 2859; Frost, *Annalen*, *loc. cit.*): αβ-diphenylpropiononitrile, m. p. 46° (Found: C, 87·1; H, 6·1. Calc. for $C_{15}H_{13}N$: C, 87·0; H, 6·3%); β-o-*methoxyphenyl-α-phenylpropiononitrile*, b. p. 140°/0·05 mm. (Found: C, 81·3; H, 6·5%); β-p-*methoxyphenyl-α-phenylpropiononitrile*, m. p. 89° (Found: C, 81·1; H, 6·1; N, 5·8. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3; N, 5·9%); β-3 : 4-*dimethoxyphenyl-α-phenylpropiononitrile*, m. p. 98° (Found: C, 76·5; H, 6·2; N, 5·5. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%).

β-o-*Methoxyphenyl-α-phenylpropionic Acid.*—(i) Sodium amalgam (2½%, 500 g.) was added with stirring during 3 hr. to a solution of *o*-methoxy-α-phenylcinnamic acid (30 g.), sodium hydroxide (20 g.), and water (500 c.c.). The solid, obtained by acidification of the filtered liquid at 0°, was dissolved in hot 60% ethanol, whereupon β-o-*methoxyphenyl-α-phenylpropionic acid* (18 g., 60%), m. p. 135°, crystallised (Found: C, 74·8; H, 6·35. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·25%). (ii) A mixture of β-*o*-methoxyphenyl-α-phenylpropiononitrile (10 g.), sodium hydroxide (10 g.), and ethanol (100 c.c.) was refluxed for 20 hr. and the precipitate (9·7 g., 90%) obtained on acidification was crystallised from aqueous ethanol (Found: C, 75·0; H, 6·0%). In later runs, β-*o*-methoxyphenyl-α-phenylpropionic acid was obtained directly by addition of sodium hydroxide to the solution from sodium-amalgam reduction of *o*-methoxy-α-phenylcinnamonitrile.

The following acids were similarly prepared by methods (i) and (ii) from the corresponding cinnamic acids (Funk and Kostanecki, *Ber.*, 1905, **38**, 940) or cinnamonitriles (Niederl and Ziering, *J. Amer. Chem. Soc.*, 1942, **64**, 885): αβ-Diphenylpropionic acid, m. p. 81° (Found: C, 79·7; H, 6·3. Calc. for $C_{15}H_{14}O_2$: C, 79·7; H, 6·2%); β-*m*-methoxyphenyl-α-phenylpropionic acid, m. p. 47° (Found: C, 75·3; H, 6·4. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·25%); β-*p*-methoxyphenyl-α-phenylpropionic acid, m. p. 119° (Found: C, 75·4; H, 6·25%); β-3 : 4-dimethoxyphenyl-α-phenylpropionic acid, m. p. 98° (Found: C, 71·2; H, 6·3. Calc. for $C_{17}H_{18}O_4$: C, 71·3; H, 6·3%).

The following acids were prepared by method (ii) only : α-*p*-Methoxyphenyl-β-phenylpropionic acid, m. p. 108° (Found : C, 75·3; H, 6·3. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·25%); α-m-*methoxyphenyl*-β-*phenylpropionic acid*, m. p. 48° (Found : C, 75·1; H, 6·3%); α-3 : 4-*dimethoxyphenyl*-β-*phenylpropionic acid*, m. p. 137° (Found : C, 71·3; H, 6·4. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%), αβ-*bis*-3 : 4-*dimethoxyphenylpropionic acid*, m. p. 136° (Found : C, 65·8; H, 6·4. $C_{18}H_{18}O_5$ requires C, 65·7; H, 6·6%).

2-Phenylindan-1-one.—αβ-Diphenylpropionic acid (15 g.) was quickly added with vigorous shaking to a mixture of phosphoric acid (*d* 1·75; 120 g.) and phosphoric oxide (120 g.) at 170°. When the mixture had cooled it was poured into water, and the crude product (9 g.; 60%) was isolated by extraction with ether. It was characterised as the oxime, m. p. 159° (Found : C, 80·5; H, 6·1. Calc. for $C_{15}H_{13}ON$: C, 80·7; H, 5·8%). Similarly the following indan-1-ones were prepared from the corresponding propionic acids (the temperature of the mixture during addition, and the yield obtained are given in parenthesis) : 5-Methoxy-2-phenyl- (160°; 40%), m. p. 110°, from ethanol (Morris, *J.*, 1950, 1913, gives m. p. 115°) (Found : C, 80·5; H, 6·1. Calc. for $C_{16}H_{14}O_2$: C, 80·7; H, 5·9%); *oxime*, m. p. 190° (Found : C, 76·0; H, 6·1; N, 5·6. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%). 6-*Methoxy-2-phenyl-* (187°; 20%), m. p. 153° (Found : C, 80·8; H, 6·0%); *oxime*, m. p. 154° (decomp.) (Found : C, 76·3; H, 6·1%). 5 : 6-*Dimethoxy-2-phenyl-* (160°; 30%), m. p. 156° (Found : C, 76·0; H, 5·7. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); *oxime*, m. p. 202° (decomp.) (Found : C, 72·2; H, 6·4. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0%). 5 : 6-Dimethoxy-2-phenylindan-1-one was also obtained by refluxing β-3 : 4-dimethoxyphenyl-α-phenylpropionic acid (8 g.), phosphoric oxide (80 g.), and benzene (300 c.c.) for 1 hr., pouring the mixture on ice, and isolating the product (6 g.) from the dried benzene extract.

1-Amino-5-methoxy-2-phenylindane (cf. Braun and Manz, *Ber.*, 1929, **62**, 1059). Sodium-amalgam (2½%; 100 g.) was added during 1 hr. to a stirred solution of 1-hydroxyimino-5 methoxy-2-phenylindane (5 g.) in ethanol (60 c.c.) and acetic acid (10 c.c.), the liquid was poured into water, and the mixture acidified with hydrochloric acid. The crude product was isolated with ether and distilled, the fraction (1·7 g.), collecting at 160°/0·15 mm., was dissolved in ether, and hydrogen chloride passed through the solution to precipitate *1-amino-5-methoxy-2-phenylindane hydrochloride* (1·9 g.), m. p. 126° (Found : N, 4·9; Cl, 12·5. $C_{16}H_{18}ONCl$ requires N, 5·1; Cl, 12·9%).

The following were prepared similarly : *1-Amino-6-methoxy-2-phenylindane hydrochloride*, m. p. 210° (decomp.) (Found : C, 69·2; H, 6·3. $C_{16}H_{18}ONCl$ requires C, 69·7; H, 6·3%); *1-amino-5 : 6-dimethoxy-2-phenylindane hydrochloride*, m. p. 210° (Found : C, 66·3; H, 6·5; N, 4·6. $C_{17}H_{20}O_2$ requires C, 66·7; H, 6·5; N, 4·6%).

1-Bromo-2-phenylindene.—A solution of 2-phenylindene (5 g.) and *N*-bromosuccinimide (4·6 g.) in carbon tetrachloride (50 c.c.) was refluxed for 30 min., the solvent evaporated after filtration, and the residue dissolved in hot aqueous ethanol (80%). When the solution cooled *1-bromo-2-phenylindene* (4·8 g., 67%), m. p. 124°, crystallised (Found : Br, 29·2. $C_{15}H_{11}Br$ requires Br, 29·6%).

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University Science Laboratories, South Road, Durham. [*Received, January 7th*, 1954.]

Bond Orders in Dibenzo[cd,lm]*perylene.**

By E. Theal Stewart.

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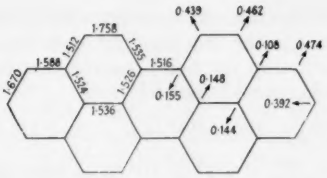
Calculation of the bond orders and the free valences in dibenzo[*cd,lm*]perylene by the method of molecular orbitals (Coulson, " Valence," Oxford University Press, 1952, Ch. 9) gives the results shown in the molecular diagram, bond order being shown on the left and free valences on the right.



In the ground state the highest occupied and the lowest vacant orbitals have the binding energies $\varepsilon = 0{\cdot}285\beta = 0{\cdot}266\gamma$ (b_{1g}), and $\varepsilon = -0{\cdot}285\beta = -0{\cdot}307\gamma$ $(b)_{3u}$), the overlap integral between adjacent carbon atoms being taken as 0·25. [β, γ, and the symmetry notation are as defined by Coulson (*Proc. Phys. Soc.*, 1948, **60**, 257). The *X*-axis is normal to the molecular plane; the *Y*-axis and the *Z*-axis are respectively the long and the short axes of the molecule.] Dibenzo[*cd,lm*]perylene may be assumed to have the symmetry $V_h \equiv D_{2h}$, and the electronic transition $b_{1g} \longleftrightarrow b_{3u}$ $(A_{1g} \longleftrightarrow B_{2u})$ is thus allowed with ***y*** polarization.

On the basis of the empirical relation $\gamma = -2{\cdot}3 \times 10^4$ cm.$^{-1}$ (Platt, *J. Chem. Phys.*, 1950, **18**, 1168), this transition should correspond to a first absorption band (*i.e.*, lowest-energy band) at about 750 mμ. However, the first absorption band of peropyrene, which Clar (*Ber.*, 1943, **76**, 458) has formulated as dibenzo[*cd,lm*]perylene, is at about 440 mμ. The simple molecular-orbital method gives notably inexact results in the calculation of the absolute values of transition energies; but the discrepancy between theory and experiment in the present case seems surprisingly large. There is little reason for supposing that peropyrene has a structure other than that which Clar proposed; but it is as well to note that the evidence for his formulation consists solely of (*a*) the one-stage synthesis of peropyrene from perinaphthenone [or from perinaphthane-4-carboxylic acid (Alder and Wolff, *Annalen*, 1952, **576**, 182)]; and (*b*) an indecisive combustion analysis.

It is perhaps significant that peropyrene is exceptional in giving an exceedingly poor result (624 mμ) in the normally successful perturbation method which Dewar (*J.*, 1952, 3532) introduced for calculating the wave-length of the first absorption band of condensed polynuclear aromatic hydrocarbons. In Dewar's method the molecule is supposed to be dissected into two odd-membered radicals; the non-bonding molecular orbital of each radical is expressed in the usual way as a linear combination of atomic orbitals; and the transition energy is then obtained as a function of the coefficients of the atomic orbitals at the points of dissection. Dewar suggested that the failure of his calculation in the case of peropyrene was due to the assumption of a uniform value for the various resonance integrals, the value for the " lateral " bonds probably being abnormally high (the bond order is in fact shown to be 1·758 in the present calculation). On repeating his calculations using the arbitrary values $\sqrt[8]{2}\,\beta$ for the lateral bonds, $\beta/\sqrt[8]{2}$ for the bonds adjacent to the lateral bonds, and β for all other bonds, he obtained the value 457 mμ for the wave-length of the first absorption band, in remarkable agreement with the experimental result, quoted as 458 mμ. It would seem, however, that this agreement is purely fortuitous; for a further refinement of Dewar's calculations, in which *all* the resonance integrals are adjusted in accordance with the calculated bond orders, gives the value 573 mμ. More-

* Ring Index No. 3841.

over, on applying Dewar's method to other molecules containing individual bonds of high order, again adjusting all the resonance integrals to correspond with the bond orders, one obtains results which are in general in poorer agreement with experiment than those Dewar obtained by using the uniform value β. For example :

	Observed mμ	Calc. (uniform value for resonance integrals) mμ	Calc. (values of resonance integrals adjusted) mμ
Phenanthrene	293	328	277
3 : 4-Benzophenanthrene ...	317	284	274
Pyrene	364	360	337

The relative values (β′) of the various resonance integrals used in calculating the coefficients of the atomic orbitals in the non-bonding molecular orbitals were obtained from the bond orders by first calculating the bond lengths (Coulson, *Proc. Roy. Soc.*, 1951, *A*, **207**, 91), and then using the Lennard-Jones relation,

$$2\beta' = W_d - W_s + \tfrac{1}{2}K_d(r - r_d)^2 - \tfrac{1}{2}K_s(r - r_s)^2,$$

with $W_d - W_s = -54{\cdot}4$ kcal., $K_d = 9{\cdot}57 \times 10^5$ dyne/cm., and $K_s = 4{\cdot}50 \times 10^5$ dyne/cm. (Coulson and Altmann, *Trans. Faraday Soc.*, 1952, **48**, 293). In calculating the transition energies, Dewar's value of β (determined empirically from the absorption spectrum of benzene) was taken to be equal to the value of β′ corresponding to a bond order of 1·667 (the bond order in benzene).

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MATHEMATICAL INSTITUTE, 10, PARKS ROAD, OXFORD. [*Received, December* 21*st*, 1953.]

Some Experiments Relating to the Chemistry of the Dichlorohydrins.

By P. B. D. DE LA MARE and J. G. PRITCHARD.

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CHARACTERISATION of the isomeric dichlorohydrins, 2 : 3-dichloropropan-1-ol and 1 : 3-dichloropropan-2-ol, was difficult until Lennart Smith (*Z. physikal. Chem.*, 1917, **92**, 740) showed that the two isomers can best be distinguished by their rates of reaction with alkali. In a current investigation, it was desired to prepare 2 : 3-dichloropropan-1-ol labelled with ^{36}Cl in one of the two possible positions. The route adopted was the following, in which the second stage is, so far as we are aware, a new example of a well-known reaction :

$$CH_2{:}CCl{\cdot}CO_2H \xrightarrow{H^{36}Cl} {}^{36}Cl{\cdot}CH_2{\cdot}CHCl{\cdot}CO_2H \xrightarrow{LiAlH_4} {}^{36}Cl{\cdot}CH_2{\cdot}CHCl{\cdot}CH_2{\cdot}OH \quad . \quad . \quad (1)$$

It was considered unlikely that rearrangement would occur in either stage, and this was confirmed by treating the [3-^{36}Cl]-2 : 3-dichloropropan-1-ol with aqueous alkali. Pure epichlorohydrin was isolated from the product, and contained, within 3%, all of the ^{36}Cl:

$$^{36}Cl{\cdot}CH_2{\cdot}CHCl{\cdot}CH_2OH \xrightarrow{NaOH\text{–}H_2O} {}^{36}Cl{\cdot}CH_2{\cdot}\underset{\diagdown O \diagup}{CH}{\cdot}CH_2 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Activity, 48·3 ± 1·0 counts l. mole^{-1} min.$^{-1}$ Activity, 46·8 ± 1·2 counts l. mole^{-1} min.$^{-1}$

In preliminary experiments, it was shown that if 2 : 3-dichloropropan-1-ol is allowed to react to completion with one equivalent of alkali at 0° the sodium chloride produced in the reaction does not all come from the central carbon atom. This would be difficult to understand if epichlorohydrin were the sole organic product of reaction ; and, in fact, when the reaction is carried out on a preparative scale, epichlorohydrin can be obtained only in about 50% yield It seems likely, from its known reactions (*e.g.*, with phenols in alkaline

solution, to give ethers of the type $CH_2 \cdot CH \cdot CH_2 \cdot OR$ (O); cf. Boyd and Marle, *J.*, 1908, **93**, 839; 1909, **95**, 1807; 1910, **97**, 1788) that epichlorohydrin would condense with any alcohols present in alkaline solution. Consistently, there was isolated from the products of the reaction of 2 : 3-dichloropropan-1-ol with alkali a fraction containing complex high-boiling products.

After reaction of 2 : 3-dichloropropan-1-ol with $Li^{36}Cl$ in anhydrous acetone at 65° for four days, 76% of the introduced ^{36}Cl was in the 3-, and the remainder in the 2-position, as is consistent with the expectation that the 2-position would be considerably hindered sterically for bimolecular substitution. The difference in rate of bimolecular attack at the two positions is not, however, sufficiently great for the reaction to be useful for the specific labelling of the 3-position.

Experimental.—Radioactive hydrochloric acid and lithium chloride were obtained from potassium chloride which had been irradiated by a high flux of neutrons at the Atomic Energy Research Establishment, Harwell, Didcot, Berks. We are indebted to this organisation for their co-operation in providing this specimen. Radioactivity was measured with the conventional type of liquid counter made by Twentieth Century Electronics Ltd., most of whose counters were found to have walls sufficiently thin to allow the passage of the weak β-radiation from ^{36}Cl. Amplifying, scaling, and recording units were commercial models. All counts recorded here are corrected for a background of about 10 counts min.$^{-1}$.

Pure 2 : 3-dichloropropan-1-ol was prepared by fractionation of commercial dichlorohydrin; it had b. p., 182°/760 mm., 71·7—72·2°/10 mm., n_D^{25} 1·4822. Its reaction with sodium hydroxide (both reactants 0·05N) had k_2 = 0·0100 l. mole^{-1} min.$^{-1}$ at 0·0°, and 0·32 l. mole^{-1} min.$^{-1}$ at 25·0°; no systematic trend in the rate-coefficients was observed, and the absence of any appreciable rapid initial reaction showed the absence of the isomeric dichlorohydrin.

Pure 1 : 3-dichloropropan-2-ol was prepared by the reaction of hydrochloric acid with epichlorohydrin (cf. Hill and Fisher, *J. Amer. Chem. Soc.*, 1922, **44**, 2586). Fractionation gave a product of b. p. 172°/760 mm., n_D^{25} 1·4810. Its reaction at 0·0° with sodium hydroxide (both reactants 0·05N) had k_2 = 2·12 l. mole^{-1} min.$^{-1}$, constant within experimental error over the 68% reaction followed.

α-Chloroacrylic acid was prepared by the following method (Imperial Chemical Industries Ltd., Fr.P. 845,230/1939; cf. *Chem. Abs.*, 1941, **35**, 1070, 7975). Trichloroethylene was condensed with paraformaldehyde in the presence of concentrated sulphuric acid and copper bronze. Steam-distillation gave a lower layer of an oil, which was dissolved in ether. When the ether was allowed to evaporate *in vacuo*, the oil solidified to a material, m. p. 63—65° (lit., 64°). The crude oil was found suitable for the preparation of αβ-dichloropropionic acid by the following method (cf. Werigo and Melikov, *Ber.*, 1877, **10**, 1499). Dry hydrogen chloride (9·8 g.), containing a suitable amount of $H^{36}Cl$, was dissolved in acetic acid (100 ml.), and to this was added α-chloroacrylic acid (22·4 g.). After reaction had proceeded for 64 hr. at 45°, the product was fractionated, giving 15 g. of material, b. p. 114—118°/14·5 mm., which solidified and on recrystallisation from light petroleum gave [β-^{36}Cl]-αβ-dichloropropionic acid, m. p. 51·5—53° (lit., 50°) (Found: C, 25·2; H, 2·8. Calc. for $C_3H_4O_2Cl_2$: C, 25·2; H, 2·8%). αβ-Dichloropropionic acid was reduced as follows. To the acid (17·5 g.) in dry ether (70 ml.) was added lithium aluminium hydride (4·5 g.) in dry ether (100 ml.). The mixture was refluxed for 15 min. and then treated with 2N-sulphuric acid (250 ml.). The ethereal layer was dried (K_2CO_3, then Na_2SO_4) and fractionated, giving [3-^{36}Cl]-2 : 3-dichloropropan-1-ol (7 g.), b. p. 78—79°/13 mm., n_D^{25} 1·4822 (Found: C, 27·7; H, 4·85. Calc. for $C_3H_6OCl_2$: C, 27·9; H, 4·7%). Its reaction with sodium hydroxide (both reactants 0·05N) had k_2 = 0·32 l. mole^{-1} min.$^{-1}$ at 25·0°. No systematic trend in the rate-coefficients was observed, and the absence of any appreciable rapid initial reaction showed the absence of the isomeric dichlorohydrin.

To prepare epichlorohydrin from this material, it was first diluted by the addition of 8·08 g. of inactive 2 : 3-dichloropropan-1-ol to 4·57 g. of the active material. The diluted sample was treated with N-sodium hydroxide (99 ml.) for 18 hr. at 0°. The product was extracted with ether, and the extract was dried (Na_2SO_4) and fractionated, giving 2 ml., b. p. 117—118°/760 mm., n_D^{25} 1·4358 (Found: C, 38·9; H, 5·6. Calc. for C_3H_5OCl: C, 38·9; H, 5·4%). A specimen of this material (1·483 g., in 10 ml. of alcohol) had a count of 75·1 per min. The undiluted 2 : 3-dichloropropan-1-ol (1·176 g., in 10 ml. of alcohol) had a count of 121·6 per min. From these values can be calculated the activities recorded in connection with equation (2);

they are arbitrary, since they depend on the thickness of the wall of the counter; and are the actual number of counts per minute given by a molar solution.

When inactive 2 : 3-dichloropropan-1-ol (50 g.) was allowed to react with 1·00N-sodium hydroxide (390 ml.) at 0° for 23 hr., there were obtained (*a*) epichlorohydrin (17 g.), b. p. 117—122°, n_D^{25} 1·4365, (*b*) *ca.* 0·2 g., b. p. 122—170°, n_D^{25} 1·4498, and (*c*) *ca.* 7 g., b. p. 90—100°/18 mm., n_D^{25} 1·4778. This relatively high-boiling material (*c*) was a complex mixture, and was not investigated further. The smallness of fraction (*b*) excludes the formation in this reaction of any substantial amount of β-epichlorohydrin, b. p. 135°, or of the possible products of dehydrochlorination, 3-hydroxy-1- or -2-chloroprop-1-ene, b. p. 149° and 136° respectively. A separate experiment showed that some of the sodium chloride released in the reaction came from the 3-carbon atom. [3-^{36}Cl]-2 : 3-Dichloropropan-1-ol (1·200 g., activity 98·5 counts per min.) was allowed to react to completion with 1·00N-sodium hydroxide (9·4 ml.). The organic material and solvent were removed *in vacuo*, and the remaining salt had an activity of 22·5 counts per min.

The dehydrochlorination by aqueous alkali of [β-^{36}Cl]-αβ-dichloropropionic acid was also investigated. The acid (1·07 g.) was heated for 44 hr. at 18° and for 15 min. at 50° with 15·0 ml. (2 equivs.) of 1·00N-alkali. The product was neutralised with 1·25 ml. of 6·0N-hydrochloric acid. The water and organic acid were removed under a high vacuum. The remaining sodium chloride, dissolved in 10 ml. of water, had a count of 99·3 per min.; it was shown (Volhard) to contain 1·47N-chloride. Reaction with acidified silver nitrate for 22 hr. at 90° released no additional chloride ion, and hence the sodium chloride retained no organic chlorine compounds. The aqueous solution of the organic acid which had been removed *in vacuo* (38 ml.) had a count of 1·3 per min. It contained almost no chloride. Such a small activity is almost indistinguishable above the background, and determines an upper limit ($5 \pm 4\%$) to the extent to which dehydrochlorination of αβ-dichloropropionic acid yields β-chloroacrylic acid; the α-isomer has long been known to be the major product of this reaction (cf. Werigo and Werner, *Annalen*, 1873, **170**, 168).

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William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, December 1st*, 1953.]

A Note on the Dipole Moment of Benzyl Alcohol.

By A. D. Buckingham, H. G. Holland, and R. J. W. Le Fèvre.

[Reprint Order No. 4797.]

The measurements now recorded were started about the same time as those on sulphur dioxide, methylene dichloride, chloroform, paraldehyde, and ethylene oxide (cf. *J.*, 1950, 283, 556, 3370), and for the same reason, that benzyl alcohol, having a *negative* Kerr constant (Leiser, "Abhandlungen der Deutschen Bunsen-Gesellschaft," 1910, Nr. 4), might display a *larger* apparent dipole moment in benzene solution than the true value determined for the gaseous solute. The work was part of a programme outlined in *Trans. Faraday Soc.*, 1947, **43**, 392; its background is explained in the references just cited, and also in *J.*, 1950, 290. Benzyl alcohol was of special interest since in Leiser's list it was only surpassed by paraldehyde in the negative magnitude of its Kerr constant; Leiser's data, relatively to carbon disulphide as 100, were: paraldehyde, −713, benzyl alcohol, −477; by contrast methylene dichloride and chloroform were only −36 and −100, respectively.

The following observations have been made at widely spaced times; for each batch, benzyl alcohol was freshly fractionated and only that portion with b. p. 204·8°/760 mm. was used. General experimental details require no comment (cf. Le Fèvre, "Dipole Moments," Methuen, 3rd Edn., Chap. 2, the circuits shown as Figs. 11 and 17 being employed for the dielectric capacity measurements on the vapour and the solutions respectively) except to mention that the gas cell has been calibrated with benzene as a secondary standard, $P_{C_6H_6}$ being taken as 26·62 c.c., this being the value for liquid

benzene. Comparisons between benzene and carbon dioxide now being made here (by Mr. Narayana Rao) are yielding values of the polarisation very close to this for benzene vapour (cf. also Craven, *Proc. Phys. Soc.*, 1945, **57**, 97). A full temperature range with gaseous benzyl alcohol could not be secured owing to its decomposition (with production of coke-like material necessitating dismantlement of the cell) above about 200°. [Beilstein's " Handbuch " (Zweites Ergänzungswerk, Vol. VI, p. 406) notes the thermal breakdown of benzyl alcohol in hot glass tubes at 210—215° or over copper from 230—330° to such products as benzaldehyde, toluene, dibenzyl ether, etc.] Values of $P_{\text{gas}}^{\text{benzyl alcohol}}$ at 191° and at two lower temperatures are reported in Table 2. In the absence of a direct determination of the distortion polarisation the value 32·5 c.c. for the molecular refraction $[R_L]_D$ (Walden, *Z. physikal. Chem.*, 1907, **59**, 385) has been used to estimate both μ_{gas} and $\mu_{C_6H_6}$; this should not seriously affect their relative magnitudes. Dielectric constants, ε, and densities, d, now found for solutions containing weight fractions w_2, of benzyl alcohol in benzene at 25° are listed in Table 1.

TABLE 1. *Dielectric constants and densities of benzyl alcohol–benzene mixtures.*

10^6w_2	0	4721	9079	9270	11,480	14,510
ε_{25}	2·2725	2·2863	2·2990	2·3006	2·3062	2·3166
10^6w_2	15,020	27,250	45,280	96,850	149,900	203,840
ε_{25}	2·3182	2·3566	2·4197	2·6095	2·8321	3·1085

10^6w_2 ...	0	6130	8962	9057	12,350	12,460	14,840	15,020	31,440
d_4^{25}	0·87378	0·87463	0·87513	0·87504	0·87557	0·87555	0·87588	0·87578	0·87829
10^6w_2 ...	50,910	66,310	110,910	135,600	149,900	203,840	208,810	255,610	
d_4^{25}	0·88157	0·88394	0·89101	0·89396	0·89606	0·90343	0·90489	0·91445	

whence (cf. *J.*, 1953, 1622): $\Delta\varepsilon = (2{\cdot}90_2 \pm 0{\cdot}01_3)w_2 + 5{\cdot}81w_2^2$ and $\Delta d = (0{\cdot}142_5 \pm 0{\cdot}001_8)w_2 + 0{\cdot}047w_2^2$.

Discussion.—From Table 1 the total polarisation of benzyl alcohol at infinite dilution in benzene is found to be $89{\cdot}9 \pm 0{\cdot}3$ c.c., whence, if $[R_L]_D$ is taken as $_DP$, $\mu_{C_6H_6} = 1{\cdot}67_5 \pm 0{\cdot}00_5$ D. The three polarisations of Table 2 yield, if the same $_DP$ is used, values for μ_{gas} of 1·71, 1·70, and 1·72 D. respectively. The mean of these is 1·71 D. Evidently the

TABLE 2. *Dielectric polarisations of benzyl alcohol as a vapour.*

Temp.	$(\Delta C/p)_{p=0}^{PhCH_2\cdot OH}$	P (c.c.)	Pressure (cm.)	No. of obsns.
178·3°	41·83 *	72·00	3—5·5	11
183·3	40·74 *	70·99	3—6	7
191·0	40·13 *	71·39	3—7	7

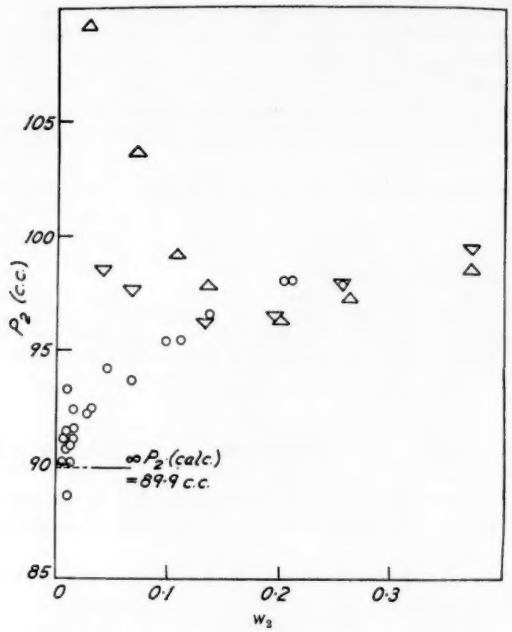
* $(\Delta C/p)_{p=0}^{C_6H_6} = -1{\cdot}798 + 7790{\cdot}0/T$.

" solvent effect " (*i.e.* the algebraic sign of $\mu_{\text{soln}} - \mu_{\text{gas}}$) is slightly negative, in contrast to that found for paraldehyde (*J.*, 1950, 290) where the ratio $\mu_{C_6H_6}/\mu_{\text{gas}}$ was definitely greater than unity. Benzyl alcohol is evidently another substance—additional to sulphur dioxide (*J.*, 1950, 283), methylene dichloride (*J.*, 1950, 556), and ethylene oxide (*J.*, 1950, 3370)—which breaks the " Kerr constant rule " of Le Fèvre and Le Fèvre (*J.*, 1935, 1747). The case is remarkable because of the largeness of the negative Kerr constant involved. It is of course possible that this is a property of *liquid* benzyl alcohol only, and arises from the presence of association complexes or aggregates whose anisotropic polarisabilities are not the same as those of the separated molecules, with which one is dealing at infinite dilution. A similar suggestion has been made for aniline (*J.*, 1949, 902).

Previous estimates of the dipole moment of benzyl alcohol (by the refractivity method) have been as follow:

	Solvent	μ, D
Williams, *Physikal. Z.*, 1928, **29**, 204	Benzene	1·66
Bodenheimer and Wehage, *Z. physikal. Chem.*, 1932, *B*, **18**, 343	Benzene	1·75
Higasi, *Bull. Inst. Phys. Chem. Res. Tokyo*, 1932, **11**, 729.....	Benzene	1·69
Fairbrother, *Proc. Roy. Soc.*, 1933, *A*, **142**, 173	Decalin	1·7
Hückel and Wenzke, *Z. physikal. Chem.*, 1942, *B*, **51**, 144	Benzene	1·45—1·89
" " " "	*cyclo*Hexane	1·76—2·03
" " " "	Carbon tetrachloride	1·67—1·76

The first four values are in reasonable accord with the μ_{gas} and $\mu_{C_6H_6}$ now found. In detail however the measurements of Table 1 present an interesting disagreement with those of Hückel and Wenzke. These authors reported that the polarisation–concentration curves of benzyl alcohol in the three solvents named changed their forms with temperature, P_2 tending to increase as infinite dilution was approached at lower temperatures, and *vice versa* (hence the variations in the apparent moments listed above). With benzene the change-over was stated to occur between 35° and 40°. After transforming molar into



weight fractions, the values of P_2 of Hückel and Wenzke at 20° and 30° are shown as points △ and ▽ respectively in the Figure: their increase as w_2 approaches zero can be seen. By contrast, when the values of ε or d missing from Table 1 are provided by interpolation from smoothed graphs of these quantities against w_2, and the mixture formula of Sugden (*Trans. Faraday Soc.*, 1934, **30**, 720) is applied, the polarisations deduced (points ○) show diminution towards infinite dilution. Beyond noting this apparent discrepancy with the observations by Hückel and Wenzke we withhold further comment pending studies in other media.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, November* 13*th*, 1953.]

The Dissociation Constant of Chlorous Acid.

By G. F. Davidson.

[Reprint Order No. 4842.]

The dissociation constant of chlorous acid is given by Latimer (" Oxidation Potentials," Prentice-Hall Inc., New York, 1938, p. 48) as 10^{-2}, a value which he deduces from the free energy of dissociation of the acid as evaluated in unpublished work by Barnett (Ph.D. Thesis, University of California, 1935). Fontana and Latimer (*J. Amer. Chem. Soc.*, 1947, **69**, 2598) quote Barnett's value for the free energy of dissociation at 25° as 2·67 kcal./mole, and this corresponds to a dissociation constant of $1{\cdot}10 \times 10^{-2}$. From measurements of pH made with the glass electrode on solutions resulting from the addition of sulphuric acid to solutions of barium chlorite, Tachiki (*J. Chem. Soc. Japan*, 1944, **65**, 346; *Chem. Abs.*, 1947, **41**, 3347) found the dissociation constant of chlorous acid at 25° to be $4{\cdot}9 \times 10^{-3}$. A third value, $1{\cdot}01 \times 10^{-2}$ at 23°, has recently been reported by Lister (*Canad. J. Chem.*, 1952, **30**, 879), but no details of the method employed are given.

A new determination has now been made in connection with an investigation involving the use of acidified chlorite solutions as oxidants for aldehyde groups in oxidized celluloses. The method employed was the potentiometric titration of solutions of sodium chlorite with hydrochloric acid by means of the glass electrode at room temperature (19—20°). The sodium chlorite was obtained by two recrystallizations of the commercial salt and dehydration of the product; its purity, determined iodometrically, was 99·8%. The titrations were performed as rapidly as possible and were stopped when one-eighth of the amount of acid equivalent to the chlorite had been added. At this point the solutions were only faintly yellow, and it is therefore probable that decomposition of chlorous acid, which takes place with formation of chlorine dioxide, chloric acid, and hydrochloric acid (cf. White, Taylor, and Vincent, *Ind. Eng. Chem.*, 1942, **34**, 782), occurred to only a slight extent.

Two titrations were performed at each of four chlorite concentrations, and the dissociation function, defined by the equation $K_a' = a_{H^+} \cdot c_{ClO_2^-}/c_{HClO_2}$, was evaluated at about ten points in each titration. The mean values obtained for pK_a' are given in the Table.

Chlorite concn., M	0·01	0·02	0·05	0·1
pK_a'	1·91	1·88	1·84	1·80
	1·92	1·88	1·84	1·81

The data are not sufficiently accurate or extensive to yield an exact value for the thermodynamic dissociation constant K_a, but by plotting pK_a' against the square root of the ionic strength and extrapolating to infinite dilution the approximate value 1·97 is obtained for pK_a. The corresponding value of K_a is $1{\cdot}07 \times 10^{-2}$, which agrees closely with that derived from Barnett's results.

British Cotton Industry Research Association,
Shirley Institute, Didsbury, Manchester.

[*Received, November 27th*, 1953.]

*The Oxidation of Phenylhydrazones. Part III.**

By B. M. Lynch and K. H. Pausacker.

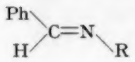
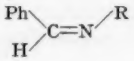
[Reprint Order No. 5034.]

Witkop and Kissman (*J. Amer. Chem. Soc.*, 1953, **75**, 1975) report that benzylazoxybenzene ($C_{13}H_{12}ON_2$), the peracid oxidation product of benzaldehyde phenylhydrazone, is reduced by aluminium amalgam forming a compound, $C_{14}H_{14}N_2$, m. p. 155° but is reduced by lithium aluminium hydride to give benzaldehyde phenylhydrazone, m. p. 158° (*idem, loc. cit.*; Part I, *J.*, 1953, 2517).

We find that the product of aluminium amalgam reduction has the characteristics described by Witkop and Kissman, but different analytical results were obtained [Found: C, 79·2; H, 6·5; N, 14·2%; *M* (Rast), 190, 199. Calc. for $C_{13}H_{12}N_2$: C, 79·5; H, 6·2; N, 14·3%; *M*, 196. Calc. for $C_{14}H_{14}N_2$: C, 80·0; H, 6·7; N, 13·3%; *M*, 210].

The compound is, therefore, isomeric but not identical with benzaldehyde phenylhydrazone, their mixed m. p. being 20° lower. When the product obtained by aluminium amalgam reduction was heated at 160° for 15 min., it was converted into normal benzaldehyde phenylhydrazone, m. p. and mixed m. p. 158°.

It appears, therefore, that the compound is a stereoisomer of benzaldehyde phenylhydrazone. Definite assignment of configuration is not possible, but since it has been shown that the *trans*-configurations of benzylideneanilines (I; R = Ar) are the stable forms (De Gaouck and Le Fèvre, *J.*, 1938, 741), and as the reduction product is converted into a more stable compound when heated, it is probably the *cis*-form (II; R = NHPh), and normal benzaldehyde phenylhydrazone is then the *trans*-form (I; R = NHPh).

(I)  (II) 

An isomer, m. p. 154°, of benzaldehyde phenylhydrazone was obtained by Bodforss (*Ber.*, 1926, **59**, 667) by fractional crystallisation of the product from benzaldehyde and phenylhydrazine.

Similar reduction of *p*-methoxybenzylazoxybenzene, *p*-benzylazoxychlorobenzene, and *p*-benzylazoxytoluene yielded the " normal " substituted benzaldehyde phenylhydrazones (identified by m. p. and mixed m. p.).

Microanalyses were performed under the direction of Dr. K. W. Zimmermann. One of us B. M. L.) is indebted to Monsanto Chemicals (Australia) Limited for a Research Scholarship.

University, Melbourne, N.3, Victoria, Australia. [*Received, January 18th*, 1954.]

* Part II, *J.*, 1954, 1131.

Reduction of Acids to Aldehydes with Formic Acid.

By Allen J. Barduhn and Kenneth A. Kobe.

[Reprint Order No. 5058.]

Davies and Hodgson (*J.*, 1943, 84) described the reduction of six acids to aldehydes by formic acid with titanium dioxide as catalyst, in yields, based on the acid consumed, of 80—90%, and with conversions of 20—40%, except for salicylic acid for which both the conversion and yield were 92%.

At least three other laboratories have failed to repeat this work. There undoubtedly is some critical factor, which neither the original authors nor we recognized, necessary for reaction. Correspondence with Davies and Hodgson eliminated some factors, but, although we tested a large variety of process conditions, possible contaminants to reactants, and various other catalysts, we have produced no trace of aldehydes. The original paper calls for heating the carboxylic acid, formic acid, and titanium dioxide catalyst in a sealed Carius tube at 250—260°. We have used a 300-c.c. stainless-steel autoclave controlled to $\pm 0{\cdot}5°$, also a Carius tube (cf. Davies and Hodgson), temperatures from 150° to 300°, and pressures from 275 to 1400 lb. in.$^{-2}$. The formic acid has been adulterated with many possible impurities.

It appears that the catalyst does not contain the missing factor, since some of the original catalyst of Davies and Hodgson was used without success. Rutile and anatase, oxides of manganese, thorium, vanadium, and cobalt precipitated on titanium dioxide were also tried unsuccessfully.

Department of Chemical Engineering, University of Texas,
Austin, Texas, U.S.A. [*Received, January 8th*, 1954.]

Organic Fluoro-compounds. Part VIII. Some Indole Derivatives.*†

By W. B. Whalley.

[Reprint Order No. 4921.]

The modified Hoesch reaction (Whalley, Part VII *) for the preparation of 2-trihalogenoacetyl derivatives of αβ-unsubstituted coumarones has been applied to indole and several of its congeners with the production in good yield of the corresponding 3-trihalogenoacetylindoles. These derivatives, particularly the trichloro-ketones, are easily convertible into the appropriate acids, thus providing a useful addition to the limited number of methods available for the preparation of indole- and *N*-substituted indole-3-carboxylic acids in general, and to the hitherto unknown *N*-alkylindole-3-carboxylic acids unsubstituted in the 2-position, in particular. Moreover, the ease of alkylation of the acidic hydrogen attached to the nitrogen atom in 3-trifluoroacetylindoles affords a convenient alternative route to *N*-alkylindole-3-carboxylic acids.

Skatole gives 2-trifluoroacetylskatole under these conditions.

Experimental.—The Hoesch reactions with the appropriate indoles were carried out as described for αβ-unsubstituted coumarones (Part VII, *loc. cit.*).

1-*Methyl*-3-*trifluoroacetylindole*. (*a*) Prepared from indole (2 g.), 3-*trifluoroacetylindole* (1·5 g.)

* Part VII, *J.*, 1953, 3479. Enquiries concerning this paper should be addressed to the author at the Department of Organic Chemistry, The University, Liverpool, England.

† Patent applications pending.

separated from methanol in prisms, m. p. 214° (Found : C, 56·5; H, 3·0; N, 6·6. $C_{10}H_6ONF_3$ requires C, 56·3; H, 3·9; N, 6·6%); it was readily soluble, without decomposition, in 2N-sodium hydroxide, and on hydrolysis during ½ hr. with boiling 25% aqueous potassium hydroxide gave indole-3-carboxylic acid (80%), m. p. and mixed m. p. 218° (decomp.). Ellinger (*Ber.*, 1906, **39**, 2519) records m. p. 218° (decomp.). Methylation by methyl iodide–acetone–potassium carbonate during 2 hr. furnished a quantitative yield of *1-methyl-3-trifluoroacetylindole* as prisms, m. p. 105°, from methanol (Found : C, 58·5; H, 3·8; N, 6·3. $C_{11}H_8ONF_3$ requires C, 58·2; H, 3·6; N, 6·2%).

(*b*) The Hoesch reaction with 1-methylindole (2 g.) gave an identical product (2 g.); hydrolysis for 2 hr. with 40% sodium hydroxide gave *1-methylindole-3-carboxylic acid* (1·5 g.), which separated from aqueous acetone in plates, m. p. 212° (decomp.) (Found : C, 68·7; H, 5·5; N, 7·7. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·2; N, 8·0%).

3-Trichloroacetylindole, obtained in 50% yield, formed plates, m. p. 235—237° (decomp.) from methanol (Found : C, 45·9; H, 2·8; N, 5·6; Cl, 40·5. $C_{10}H_6ONCl_3$ requires C, 45·8; H, 2·3; N, 5·3; Cl, 40·5%). This ketone was converted quantitatively into methyl indole-3-carboxylate by the method described in Part IV (*J.*, 1951, 665), and into indole-3-carboxylic acid by dissolution in warm 2N-sodium hydroxide.

5 : 6-*Methylenedioxyindole-3-carboxylic acid.* 5 : 6-Methylenedioxyindole (Burton and Duffield, *J.*, 1949, 78) (1 g.) furnished 5 : 6-*methylenedioxy-3-trifluoroacetylindole* (0·6 g.) in yellow plates, m. p. 268°, from aqueous methanol (Found : N, 5·7. $C_{11}H_6O_3NF_3$ requires N, 5·5%). Hydrolysis of this ketone with boiling 10% aqueous potassium hydroxide during 1 hr. gave 5 : 6-*methylenedioxyindole-3-carboxylic acid* (75% yield); purified from benzene–acetone, it formed prisms, m. p. 239—240° (decomp.) (Found : N, 6·7. $C_{10}H_7O_4N$ requires N, 6·8%).

5 : 6-*Dimethoxy-3-trifluoroacetylindole.* By Burton and Duffield's method (*loc. cit.*) condensation of veratraldehyde (14 g.) with nitromethane gave 3 : 4-*dimethoxy-ω-nitrostyrene* (10 g.) in yellow plates (from acetic acid), m. p. 142° (Found : C, 57·6; H, 5·4; N, 6·8. $C_{10}H_{11}O_4N$ requires C, 57·4; H, 5·3; N, 6·7%); this was converted by nitration into 4 : 5-*dimethoxy-ω* : 2-*dinitrostyrene* (7 g.), yellow prisms, m. p. 173° from acetic acid (Found : C, 47·6; H, 4·0; N, 11·0. $C_{10}H_{10}O_6N_2$ requires C, 47·3; H, 4·0; N, 11·0%). Simultaneous reduction and cyclisation of the latter styrene (6 g.) gave 5 : 6-dimethoxyindole (3 g.), m. p. 158° (Oxford and Raper, *J.*, 1927, 417, record m. p. 154—155°), which furnished 5 : 6-*dimethoxy-3-trifluoroacetylindole* (1·5 g.) in yellow flat needles, m. p. 207°, from methanol (Found : N, 5·5. $C_{12}H_{10}O_3NF_3$ requires N, 5·1%).

Derivatives of 7-methylindole. This indole (2 g.) gave *7-methyl-3-trifluoroacetylindole* (1·2 g.) in yellow plates, m. p. 214°, from methanol (Found : C, 58·7; H, 3·7; N, 6·3. $C_{11}H_8ONF_3$ requires C, 58·2; H, 3·6; N, 6·2%). The ketone was easily soluble in 2N-sodium hydroxide without decomposition but when boiled with 5N-sodium hydroxide furnished 7-methylindole-3-carboxylic acid, m. p. 234° (decomp.). Kruber (*Ber.*, 1926, **59**, 2752) records m. p. 228° (decomp.). During 3 hr. in boiling acetone–potassium carbonate–benzyl bromide this ketone gave quantitatively *1-benzyl-7-methyl-3-trifluoroacetylindole*, which separated from methanol in prisms, m. p. 140° (Found : C, 68·3; H, 4·5; N, 4·5. $C_{18}H_{14}ONF_3$ requires C, 68·1; H, 4·4; N, 4·4%). This was insoluble in 2N-sodium hydroxide but dissolved rapidly in warm 20% aqueous alcoholic potassium hydroxide, to furnish quantitatively *1-benzyl-7-methylindole-3-carboxylic acid* as prisms, m. p. 241° (decomp.), from acetone (Found : C, 76·8; H, 5·7. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·7%).

7-Methyl-3-trichloroacetylindole. The addition during 20 min. of a solution of 7-methylindole (2 g.) in ether (25 ml.) to ether (100 ml.) containing zinc chloride (2 g.) and trichloromethyl cyanide (10 g.) previously saturated with hydrogen chloride at 0° gave an immediate yellow precipitate of the ketimine complex which, upon separation 24 hr. later and hydrolysis, furnished *7-methyl-3-trichloroacetylindole* in plates, m. p. 202°, from methanol (Found : C, 48·9; H, 3·3; N, 5·0; Cl, 38·0. $C_{11}H_8ON_3Cl_3$ requires C, 48·0; H, 2·9; N, 5·1; Cl, 38·7%). This ketone was converted quantitatively into the corresponding acid and methyl ester.

1 : 2-*Dimethylindole-3-carboxylic acid.* 2-Methylindole (2 g.) gave *2-methyl-3-trifluoroacetylindole* (1 g.) in prisms, m. p. 152°, from aqueous methanol (Found : C, 58·5; H, 3·9; N, 6·2. $C_{11}H_8ONF_3$ requires C, 58·2; H, 3·6; N, 6·2%). Methylation gave quantitatively 1 : 2-*dimethyl-3-trifluoroacetylindole* in plates, m. p. 115°, from methanol (Found : C, 60·1; H, 5·1. $C_{12}H_{10}ONF_3$ requires C, 60·0; H, 4·1%); this was hydrolysed to 1 : 2-dimethylindole-3-carboxylic acid, m. p. 220° (decomp.). King and L'Ecuyer (*J.*, 1934, 1901) record m. p. 217° (decomp.).

2-*Trifluoroacetylskatole*. Skatole (2 g.) gave this *ketone* (1·1 g.) in yellow prisms, m. p. 116°, from aqueous methanol (Found: C, 58·3; H, 3·5; N, 6·2. $C_{11}H_8ONF_3$ requires C, 58·2; H, 3·6; N, 6·2%); it was hydrolysed quantitatively to 3-methylindole-2-carboxylic acid, m. p. 166° (Found: C, 68·6; H, 5·2. Calc. for $C_{13}H_9O_2N$: C, 68·4; H, 5·2%).

Analyses of the fluorine-containing compounds were by the Clark Microanalytical Laboratories, Urbana, Illinois; the remainder were by Mrs. Rita Preis, Miss Doris Aitkin, and Miss Sally Haws.

SMITH, KLINE & FRENCH LABORATORIES,
PHILADELPHIA, PA.

[*Received, December 23rd,* 1953.]

OBITUARY NOTICES.

ERNEST HAROLD FARMER.

1890—1952.

ERNEST HAROLD FARMER was born on March 3rd, 1890, at Longford—a village in the agricultural district of west Derbyshire. His education he received at the Municipal School, Derby, and later at the University College, Nottingham, where he studied chemistry under Professor F. S. Kipping, F.R.S., graduating B.Sc. in 1911.

He chose teaching as a career and held appointments first at Daventry Grammar School and then at the Municipal School, Bury (Lancs.); but the incident at Sarajavo in 1914 changed the course of his whole life. He immediately volunteered for military service, entered the Inns of Court O.T.C., and was gazetted in 1915 to the Loyal North Lancashire Regiment in which he served until his demobilisation in 1919. He fought in Flanders until in 1917 at the Battle of Messines he was severely wounded in the head and right arm. The elbow joint had to be excised, and the severed ulnar nerve had to be sutured leaving him with partial paralysis of his right hand, whilst his head injuries left him partially deaf. After alternating between hospital and convalescent home for nearly two years, he was seconded for service with the Ministry of Munitions and returned to work at his old College under Professor Kipping. In 1919 he was still in uniform when he went to the Imperial College of Science and Technology (Royal College of Science) to start his researches in the organic laboratories of Professor J. F. Thorpe, C.B.E., F.R.S.

His boyhood recreations, which centred round playing the violin and church organ, were now no longer available and Farmer devoted himself whole-heartedly to his research, working long hours into the night. He graduated M.Sc. and D.I.C. in 1921 and was awarded the D.Sc. (London) in 1924 for his Thesis entitled " Some Aspects of Conjugation."

The same year he was appointed to the teaching staff of the Royal College of Science and was placed in charge of the Wiffin Laboratory (organic preparations in semi-scale plant) with Assistant Professor Martha A. Whiteley, the late Dr. G. A. R. Kon (subsequently Professor at the Chester Beattie Hospital) and Dr. (now Professor) R. P. Linstead as his colleagues. The Department of Organic Chemistry under the jovial Professor Jocelyn Thorpe was a happy one. Farmer soon gathered round him a small group of enthusiastic research students, and the congenial atmosphere of the laboratories was only marred by the lachrymation from brominated butadiene.

It was against this background that Farmer was able to set aside the disasters of war. A dinner and a show in town with his research students were not infrequent, and he enjoyed an evening of recorded classical music or singing around the piano old English songs, whilst every summer saw him on the Continent for a few weeks.

Farmer was very friendly with his students and took a real interest in their extra-mural activities and maintained this long after they had left his laboratories. When research assignments dictated their working well into the night, Farmer would generally look in the laboratory to say a cheery word at anytime between midnight and dawn. It was quite apparent, however, that the sufferings of war could not be entirely forgotten. He found it difficult to shake out bulky solutions for which he sought the willing help of his research students; and before he went into lectures an arm support had to be laced on to assist his writing on the black-board. Only a few knew of these disabilities, and the writer has hesitated to record these facts which Farmer so carefully concealed. It was characteristic of Farmer not to solicit sympathy. He was a man of straightforwardness and entire lack of any form of pretence or falsity.

In 1930 he married one of his research students, Miss Marjorie J. Wilson-Smith, at St. Luke's, Redcliffe Square.

In 1932 Farmer was invited by the Rubber Growers' Association to undertake a series of investigations on the chemical modifications of rubber with the object of producing semi-artificial materials suitable for use in industry. These studies were carried out concurrently with teaching duties and academic research. In 1938 he joined the newly formed Research Association of the British Rubber Producers as senior chemist. For the first year of his appointment he occupied the small Armstrong Laboratory at the Imperial College where he collected a small staff of four (Dr. G. F. Bloomfield and Messrs. Grey, A. Sundralingam, and D. A. Sutton).

He immediately embarked on ambitious projects of fundamental importance to rubber chemistry. In **1939** he moved with his staff to the new laboratories of the British Rubber Producers Research Association at Welwyn Garden City where he rapidly built up the new organic research laboratories. Within two years he was promoted to Assistant Director in which capacity he remained until ill health enforced his retirement.

In spite of his administrative responsibilities at B.R.P.R.A., Farmer always resisted the tendency to become a " desk-chemist " and he was perhaps happiest in opening up a new field of work by his initial experiments for his team to develop in detail. He was never in a hurry to publish and, although this sometimes exasperated his team, Farmer's published works contain few incorrect conclusions. He was friendly and helpful to his assistants and an excellent teacher of research methods. In later years he seldom took a holiday and had no patience with trade-union hours or what he believed to be the levelling down of a socialistic state.

" Distinguished for experimental studies of complex hydrocarbons and related natural products," Farmer was elected in **1948** a Fellow of the Royal Society. Unfortunately his health was already failing and in **1951** he was forced to relinguish his Assistant Directorship. His outstanding service, however, received recognition from the Association and he was appointed a Research Fellow and so he maintained his interest in its work to the end.

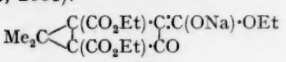
Apart from his love of music, which he derived from his early days as choir-boy, Farmer was very interested in gardening. He had planned to grow roses in his retirement and it was no little disappointment when he realised that this was to be impossible.

Farmer collapsed suddenly on Sunday, April 13th, **1952**, as he was preparing to go to Church, and was buried in the picturesque little village church of Aldenham, Herts.

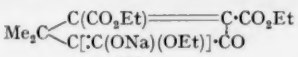
To his widow who assisted him so ably in home and laboratory must go the assurances that he was greatly esteemed by all who knew him, and the greatness of his work will be his permanent memorial.

Farmer published with his collaborators over one hundred scientific papers, mostly in the *Journal*, and contributed to various books. He wrote the whole of the Aliphatic Division of Organic Chemistry for four consecutive years (**1930—33**)—a task which was later divided—and the chapter on polymerisation (**1935**) for the Annual Reports on the Progress of Chemistry.

Farmer started, as a research student, the reinvestigation with Thrope and Ingold (*J.*, **1920**, **117**, 1362; **1922**, **121**, 128) of the structure of the yellow *bicyclo*pentane (I), which Toivonen considered to be a *cyclo*pentene (II). The existence of a dynamic equilibrium was amply illustrated; and the concept of intra-annular tautomerism contributed later to the aromatic theory and dovetailed into another series of researches led by Ingold, and in which Farmer participated, on the conditions underlying the formation of unsaturated and cyclic compounds (*J.*, **1921**, **119**, 2001).

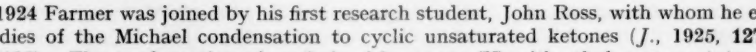


(I)



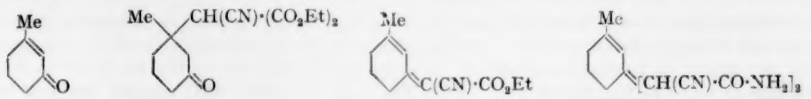
(II)

The study of the chemistry of the muconic acids by Farmer himself (*J.*, **1922**, **121**, 2015; **1923**, **123**, 2531, 3324; cf. also *J.*, **1931**, 1762) followed naturally from his initial researches. This resulted in the explanation of the 1 : 3-type of addition of ethyl cyanoacetate to muconic acid ester (III) to give (IV) as due to a primary 1 : 2-addition followed by a double $\alpha\beta : \beta\gamma$ change, and led furthermore to an attempt to synthesise substances having the Ladenburg formula (*J.*, **1923**, **123**, 3332).



(III) (IV)

In **1924** Farmer was joined by his first research student, John Ross, with whom he extended his studies of the Michael condensation to cyclic unsaturated ketones (*J.*, **1925**, **127**, 2358; **1926**, 3233). The condensation of methyl*cyclo*hexenone (V) with ethyl cyanoacetate gave the



(V) (VI) (VII) (VIII)

normal Michael addition product (VI), but the Knoevenagel condensate (VII) was found as a by-product. The treatment of this compound (VII) with ammonia, in an attempt to prepare

the amide, gave compound (VIII), the formation of which was explained as the reversion of a portion of the cyclic ester into its generators with the subsequent αβ-addition of the liberated cyanoacetic ester to the undecomposed portion. The interpretation of this chance observation as an αβ-addition was at variance with the addition of malonic ester to methyl sorbate reported as an αδ-addition compound (IX) many years previously by Vorländer (*Annalen*, **1906**, **345**, 227). Farmer (*J.*, **1927**, 1060) confirmed initially Vorländer's observations; but in view of his findings on the additive behaviour of butadienoid hydrocarbons with bromine and hydrogen (see below) he restudied the Michael reaction on sorbic ester (*J.*, **1930**, **1610**) and successfully demonstrated the presence of the αβ-product (X). He extended the study to include triene esters and the effect of substitution on the proportion of isomerides (*J.*, **1933**, **960**; **1931**, **1904**, **2561**), which did much to establish the mechanism of the Michael reaction in particular and to throw light on the anionotropic reactions.

$CH_3{\cdot}CH[CH(CO_2Me)_2]{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2Me$ (IX) $\qquad$ $CH_3{\cdot}CH{:}CH{\cdot}CH(CH_2{\cdot}CO_2Me){\cdot}CH(CO_2Me)_2$ (X)

The question of the division of the addendum of the Michael reaction was successfully resolved from a study of the addition of malonic esters to acetylenic esters (*J.*, **1936**, 1804). The yellow sodio-derivative (XI) which was alkylated and hydrolysed only with difficulty to (XII) and (XIII) respectively, revealed the components as Na and $CR(CO_2Et)_2$.

$$EtO_2C{\cdot}C{:}CR + \overbrace{CR'(CO_2Et)_2}^{Na} \longrightarrow \overbrace{EtO_2C{\cdot}C{:}CR{\cdot}CR'(CO_2Et)_2}^{Na}$$

$$EtO_2C{\cdot}CR''{:}CR{\cdot}CR'(CO_2Et)_2 \ (XII) \quad \longleftarrow \quad (XI) \quad \longrightarrow \quad EtO_2C{\cdot}CH{:}CR{\cdot}CR'(CO_2Et)_2 \ (XIII)$$

Farmer was necessarily influenced by the chemical thought being developed at the organic school in South Kensington. The Thorpe–Ingold strain theory undoubtedly led him to study the effect of *gem*-dimethyl groups on the formation and stability of anhydrides (*J.*, **1926**, **2381**; **1927**, 680) and the dipole moments of 1 : 1-dicarboxylic esters (*J.*, **1933**, **1904**), and it was not unnatural that he should extend Thorpe's classical researches on the glutaconic acids (*J.*, **1926**, **2171**; **1927**, 59).

The activities of Farmer's laboratory were, however, soon narrowed to a systematic study of the properties of conjugated compounds. The bromination of hexatriene, butadiene, and cyclic butadienes (*J.*, **1927**, **2937**; **1928**, **729**; **1929**, 172) revealed 1 : 2-addition as well as terminal addition, whilst similar experiments with dimethylbutadienes indicated the significance of substitution on the proportions of the isomerides (*J.*, **1930**, 510).

$$CH_2{:}CH{\cdot}CH{:}CH_2 \longrightarrow CH_2Br{\cdot}CHBr{\cdot}CH{:}CH_2 + CH_2Br{\cdot}CH{:}CH{\cdot}CH_2Br$$

It was natural for Farmer not to remain satisfied with the small recorded differences in physical properties of the hydrocarbons used as his starting materials, and all during this period preparative methods for, and physical properties of, the butadienoid hydrocarbons formed a major project (*J.*, **1931**, **3221**; **1933**, **1297**, **1302**; **1937**, 1065).

Furthermore about this time Farmer included in his studies the isolation from natural oils of unsaturated acids, which were to be used later in experiments on autoxidation and thermal polymerisation. The structure of the first ketonic polyene acid, licanic acid (XIV) (*Biochem. J.*, **1935**, **29**, 631) was established, whilst licanic and *iso*licanic acids were shown to correspond to α- and β-forms of elæostearic acid (*J.*, **1935**, **1632**; cf. also *J.*, **1935**, **76**, **1630**; **1936**, 1809). The acid, m. p. 85·3°, from the oil of *Parinarium laurinum* was assigned the formula (XV) (*J.*, **1935**, 759) and was seemingly the first conjugated tetraene acid reported from vegetable or animal sources.

$CH_3{\cdot}[CH_2]_3{\cdot}[CH{:}CH]_3{\cdot}[CH_2]_4{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2H$ (XIV) $\qquad$ $CH_2Me{\cdot}[CH{:}CH]_4{\cdot}[CH_2]_7{\cdot}CO_2H$ (XV)

The further extension of these studies to include the acids from fish oils presented difficulties of separation owing to the complexity of the mixture and the heat sensitivity of the components; but the perfection, in Farmer's laboratory, of molecular distillation of the mixed methyl esters from a falling film (*J. Soc. Chem. Ind.*, **1938**, **57**, 24T; *J.*, 1938, 427) opened the way to the concentration, and elucidation of the structural features, of docosahexaenoic acid.

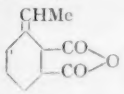
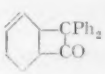
Concurrently hydrogenation experiments, initially on sorbic acid (XVI), established the 1 : 2- and 1 : 4-addition and so brought the addition of hydrogen into line with that of other

common addenda although the reaction was more complex and hydrogenated bimolecular compounds were also formed (*J.*, 1930, 522) :

$$CHMe{:}CH{\cdot}CH{:}CH{\cdot}CO_2H \quad (XVI) \longrightarrow CH_2Me{\cdot}CH{:}\dot{C}H{\cdot}CH_2{\cdot}CO_2H \text{ and } CHMe{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$$

Investigations into catalytic hydrogenation pioneered the study of selective hydrogenation (*J.*, 1932, 430; 1933, 687; 1934, 304, 1929, 1938) and drew attention to the change in additive mode from " ageing " of the catalyst. Finally additive studies of hypochlorous acid to ethylenic and butadienoid acids (*J.*, 1932, 2062, 2072) revealed the difference between hypochlorous acid, as a reagent for the ethylenic linkage *per se* which had no tendency to add *via* a carbonyl group, and hydrogen halides (cf. *J.*, 1931, 129), and permitted an assessment of the orienting influence of the carboxyl and the phenyl group (*J.*, 1933, 800, 962).

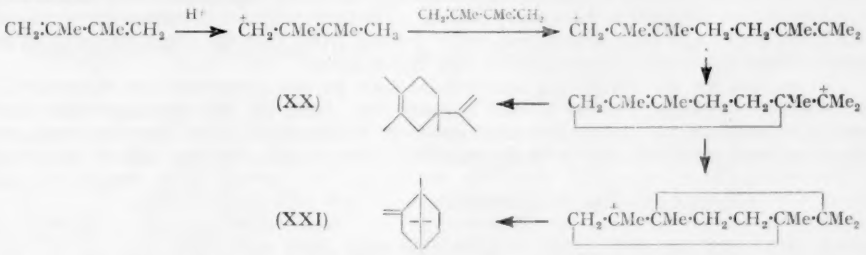
About this time Diels and Alder (*Annalen*, 1928, **460**, 98) published an interpretation of, and extended, the known reaction between benzoquinone and *cyclo*pentadiene. The significance of this reaction and the possibility of *cyclo*butane as well as *cyclo*hexene formation, corresponding to 1 : 2- and 1 : 4-dibromides, led Farmer to pursue the reaction of non-dividing addenda to conjugated systems. The Diels–Alder formula, in which the position of the double bond had been assumed, was verified. The exclusive attachment at the 1 : 4-carbon atoms to form (XVII) from hexatriene, to which bromine added at the 1 : 2- and the 1 : 6-position, was adroitly classified as configurational opportunism (*J.*, 1929, 897; *Ber.*, 1930, **63**, 360). This was later contrasted with the sole formation of a four-membered ring from diphenylketen to give (XVIII) from *cyclo*hexadiene (*J.*, 1938, 1925).

(XVII)   (XVIII)

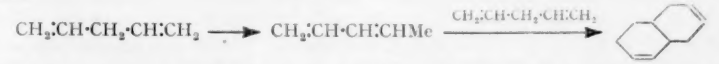
The successful studies of the reaction of dividing and non-dividing addenda with unsaturated compounds prompted consideration of the self-addition of ethylenes and butadienes. The problem of polymerisation had for many years previously forced itself on Farmer, for it was a factor affecting starting materials, and substances like hexatriene had always to be generated from their precursors immediately before they were required. Tetramethylethylene (*J.*, 1937, 1039) was first selected since it contained no hydrogen capable of transfer. The dimeride (XIX)

$$CMe_2{:}CMe_2 \longrightarrow CHMe_2{\cdot}CHMe{\cdot}CH{:}CMe{\cdot}CMe_2 \quad (XIX)$$

proved, however, no exception to Whitmore's hypothesis (*Ind. Eng. Chem.*, 1934, **26**, 94). The polymerisation of dimethylbutadiene in acid medium (*J.*, 1938, 11, 287; 1940, 1169; *Trans. Faraday Soc.*, 1939, **35**, 1034) gave a dimer of the Diels–Alder type (XX) and a crystalline dicyclic dimer (XXI), and the formation of both dimers fitted Whitmore's proton-addition mechanism :



The dimerisation of the unconjugated penta-1 : 4-diene (*J.*, 1940, 1176), which was the system occurring in several vegetable oils as well as in most glycerides from fish oils, gave some 4-allyl-3-methyl*cyclo*hexene (XXII) ; and the formation of this was explained by the prior isomerisation of one pentadiene molecule, but a hint is given that a free-radical mechanism could not be excluded.

 (XXII)

The study of the heat-polymerisation of methyl sorbate (*J.*, 1940, 1339) revealed the addition of the ·CH:CH·CO· group of one reacting molecule across the terminals of the other diene system

WILLIAM GOODWIN.

1873—1953.

Dr. William Goodwin died at his home at Wye, Kent, on December 30th, 1953.

Born in Macclesfield, Cheshire, on November 8th, 1873, he received his early education at the King Edward VI Modern Grammar School, Macclesfield (1881—1889), and Owens College, Manchester (1889—1894). After spending the next four years in analytical posts in Glasgow and Manchester, Goodwin went as Research Assistant to Professor Senier at Queen's College, Galway. From here he was awarded an 1851 Exhibition Scholarship which enabled him to study in Germany under Professor Tollens at Göttingen, and at the Laboratory for Vegetable Physiology in Paris where he worked in the field of sugar chemistry under Professor Macquenne. Goodwin then returned, first to Manchester to complete his Bachelor's degree and to carry out research in organic chemistry under Professor W. H. Perkin, jun., and then to Göttingen where he was awarded the Ph.D. degree in 1907 for a thesis entitled, "Über einige Ketone der Terpenreihe," this work having been supervised by Professor O. Wallach.

His long career in agricultural chemistry then began. After a few months as lecturer at Harper Adams College, he was appointed in 1907 to succeed Sir John Russell as head of the Chemistry Department at Wye College, Kent. Four years later he became principal of the Midland Agricultural College, Nottingham, a post which he held for eleven years; in 1922 he returned to Wye College as advisory chemist, where he remained until his retirement in 1938.

Although Goodwin became well known for his advisory work, as an examiner, and for his researches in many branches of agricultural chemistry, he always valued greatly the thorough training he had received as an organic chemist. Amongst his earlier published works are papers in the *Journal* with W. H. Perkin, jun., on such subjects as, "β-dimethylglutaric acid," "*cis*- and *trans*-hexahydro*ortho*toluic acids," "some derivatives of propionic acid, of acrylic acid, and of glutaric acid," and "the reduction of *iso*phthalic acid." Other papers, bearing also the names of Senier, Tollens, and Macquenne appear in the *Journal*, *Bull. Soc. chim.*, and *Berichte*. Goodwin, however, must be regarded above all as one of the leading influences in Britain in the development of the science of crop protection. The value of the work which he and his associates carried out over many years both on fundamental and applied aspects of insecticidal and fungicidal research will always be recognised. During this period he published many papers in *J. Agric. Sci.*, *Ann. Appl. Biol.*, and *J. S.E. Agric. Coll., Wye*, with Professor E. S. Salmon, Dr. H. Martin, and others.

Although during the last years of his life Dr. Goodwin was seriously handicapped by spinal trouble, his kind and cheerful personality was always evident and he maintained a keen interest in scientific developments, particularly in agricultural chemistry, to the end. He was a member of many learned societies and was a Fellow of the Chemical Society for fifty-seven years.

We extend our sympathy to his widow and two daughters.

R. L. Wain.

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